

# WEST Search History

DATE: Thursday, February 20, 2003

## Set Name Query

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## Hit Count Set Name

result set

*DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=OR*

L15	l14 and alpha adj 2 adj macroglobulin adj receptor	16	L15
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L14	L13 and immune near5 response	1153	L14
-----	-------------------------------	------	-----

L13	heat adj shock adj protein and fragment\$	2713	L13
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L12	alpha adj 2 adj macroglobulin adj receptor and tissue adj type adj plasminogen adj activator	4	L12
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*DB=USPT; PLUR=YES; OP=OR*

L11	l10 and alpha adj 2 adj macroglobulin adj receptor	1	L11
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L10	6239106.pn.	1	L10
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*DB=EPAB; PLUR=YES; OP=OR*

L9	WO009950303A2	1	L9
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*DB=USPT,PGPB; PLUR=YES; OP=OR*

L8	5639876.pn.	1	L8
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L7	L5 and heat adj shock adj protein	1	L7
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L6	L5 and heat shock protein	293476	L6
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L5	6403080.pn.	1	L5
----	-------------	---	----

L4	heat adj shock adj protein and alpha adj 2 adj macroglobulin	61	L4
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L3	heat adj shock adj protein near10 alpha adj 2 adj macroglobulin	2	L3
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L2	heat adj shock adj protein near10 cd91	0	L2
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L1	modulat\$ and heat adj shock adj protein near10 cd91	0	L1
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END OF SEARCH HISTORY

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NEWS 5 Apr 19 US Patent Applications available in IFICDB, IFIPAT, and IFIUDS  
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NEWS 7 Apr 22 BIOSIS Gene Names now available in TOXCENTER  
NEWS 8 Apr 22 Federal Research in Progress (FERPIP) now available  
NEWS 9 Jun 03 New e-mail delivery for search results now available  
NEWS 10 MEDLINE Reload  
NEWS 11 Jun 10 PCTFUL has been reloaded  
NEWS 12 Jul 02 FORGE no longer contains STANDARDS file segment  
NEWS 13 Jul 22 USAN to be reloaded July 28, 2002;  
NEWS 14 Jul 29 saved answer sets no longer valid  
NEWS 15 Jul 30 Enhanced polymer searching in REGISTRY  
NEWS 16 Aug 08 NETFIRST to be removed from STN  
NEWS 17 Aug 08 PHARMARKETLETTER(PHARMAML) - new on STN  
NEWS 18 Aug 08 CANCERLIT reload  
NEWS 19 Aug 10 Aquatic Toxicity Information Retrieval (AQUIRE)  
NEWS 20 Aug 19 now available on STN  
NEWS 21 Aug 19 IFIPAT, IFICDB, and IFIUDS have been reloaded  
NEWS 22 Aug 22 The MEDLINE file segment of TOXCENTER has been reloaded  
NEWS 23 Sep 03 Sequence searching in REGISTRY enhanced  
NEWS 24 Sep 03 JAPIC has been reloaded and enhanced  
NEWS 25 Sep 16 Experimental properties added to the REGISTRY file  
NEWS 26 Oct 01 CA Section Thesaurus available in CAPUS and CA  
NEWS 27 Oct 21 CASREACT Enriched with Reactions from 1907 to 1985  
NEWS 28 Oct 24 BELSTEIN adds new search fields  
NEWS 29 Oct 24 Nutraceuticals International (NUTRACEUT) now available on STN  
NEWS 30 Oct 25 MEDLINE SDI run of October 8, 2002  
NEWS 31 Nov 18 DKILIT has been renamed APOILIT  
NEWS 32 Dec 02 More calculated properties added to REGISTRY  
NEWS 33 Dec 02 TIBKAT will be removed from STN  
NEWS 34 Dec 04 CSA files on STN  
NEWS 35 Dec 17 PCTFUL now covers WP/PCT Applications from 1978 to date  
NEWS 36 Dec 17 TOXCENTER enhanced with additional content  
NEWS 37 Dec 17 Adis Clinical Trials Insight now available on STN  
NEWS 38 Dec 30 ISMEC no longer available  
NEWS 39 Jan 13 Indexing added to some pre-1967 records in CA/CAPUS  
NEWS 40 Jan 21 NUTRACEUT offering one free connect hour in February 2003  
NEWS 41 Jan 21 PHARMAML offering one free connect hour in February 2003  
NEWS 42 Jan 29 Simultaneous left and right truncation added to COMPENDEX,  
ENERGY, INSPEC  
NEWS 43 Feb 13 CANCERLIT is no longer being updated  
NEWS EXPRESS January 6 CURRENT WINDOWS VERSION IS V6.01a,  
CURRENT MACINTOSH VERSION IS V6.0b(ENGL) AND V6.00b(JP).

AND CURRENT DISCOVER FILE IS DATED 01 OCTOBER 2002  
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FILE 'HOME' ENTERED AT 15:25:49 ON 20 FEB 2003

=> file medicine, cancerlit, biosis, confaci, embase, caplus, uspatfull  
COST IN U.S. DOLLARS SINCE FILE TOTAL  
FULL ESTIMATED COST ENTRY SESSION  
0.21 0.21

FILE 'MEDLINE' ENTERED AT 15:26:27 ON 20 FEB 2003

FILE 'CANCERLIT' ENTERED AT 15:26:27 ON 20 FEB 2003

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FILE 'USPATFULL' ENTERED AT 15:26:27 ON 20 FEB 2003  
CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

=> s heat (a) shock (a) protein  
L1 72563 HEAT (A) SHOCK (A) PROTEIN

=> s 11 and alpha (a) 2 (a) macroglobulin (a) receptor  
L2 40 L1 AND ALPHA (A) 2 (A) MACROGLOBULIN (A) RECEPTOR

=> dup rem l2  
PROCESSING COMPLETED FOR L2  
L3 33 DUP REM L2 (7 DUPLICATES REMOVED)

=> d 1-33 l2b1b

L3 ANSWER 1 OF 33 USPATFULL  
ACCESSION NUMBER: 2003:40533 USPATFULL  
TITLE: Methods for the inhibition of epstein-barr virus  
transmission employing anti-viral peptides capable of  
abrogating viral fusion and transmission  
Barney, Shawn O'lin, Cary, NC, United States  
Lambert, Dennis Michael, Cary, NC, United States

INVENTOR(S):

PATENT ASSIGNEE(S) :  
Petteway, Stephen Robert, Cary, NC, United States  
Trimetris, Inc., Durham, NC, United States (U.S.  
corporation)

PATENT INFORMATION:  
US 6518013 B1 20030211  
US 1995-485546 19950607 (8)  
Continuation-in-part of Ser. No. US 1994-360107, filed  
on 20 Dec 1994, now patented, Pat. No. US 6017536  
Continuation-in-part of Ser. No. US 1994-255208, filed  
on 7 Jun 1994 Continuation-in-part of Ser. No. US  
1993-73028, filed on 7 Jun 1993, now patented, Pat. No.  
US 5464933

DOCUMENT TYPE:  
FILE SEGMENT:  
PRIMARY EXAMINER:  
ASSISTANT EXAMINER:  
LEGAL REPRESENTATIVE:  
NUMBER OF CLAIMS:  
EXEMPLARY CLAIM:  
NUMBER OF DRAWINGS:  
LINE COUNT:  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 2 OF 33 CAPLUS COPYRIGHT 2003 ACS  
ACCESSION NUMBER:  
DOCUMENT NUMBER:  
TITLE:

INVENTOR(S) :  
PATENT ASSIGNEE(S) :  
SOURCE:  
DOCUMENT TYPE:  
LANGUAGE:  
FAMILY ACC. NUM. COUNT:  
PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE  
WO 2002022886 A2 20020321 WO 2001-US29096 20010918  
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GR, GE, GH,  
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, NO, NZ, PL, PT,  
RO, RU, SD, SE, SG, SI, SK, SL, TJ, TW, TR, TT, TZ, UA, UG, UZ,  
VN, YU, ZA, ZW, AM, AZ, BY, BG, BR, BY, BZ, CA, CH, CN, CY,  
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, LV, MA, MR, NE, SN, TD, TG,  
AU 2001091059 A5 20020326 20010918  
US 2003013093 A1 20030116 20010918  
US 2000-23339P P 20000918  
WO 2001-US29096 W 20010918

L3 ANSWER 3 OF 33 CAPLUS COPYRIGHT 2003 ACS  
ACCESSION NUMBER:  
DOCUMENT NUMBER:  
TITLE:  
INVENTOR(S) :  
Laukkonen, Mattias; Moses, Ashlee; Fusch, Klaus;

PATENT ASSIGNEE(S) :  
Nelson, Jay; Bell, Yolanda; Heinrich, Michael; Simmen,  
Kenneth  
Ortho-McNeil Pharmaceutical, Inc., USA; Oregon Health  
& Science University  
PCT Int. Appl., 95 pp.  
CODEN: PIXXD2

DOCUMENT TYPE:  
LANGUAGE:  
FAMILY ACC. NUM. COUNT:  
PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE  
WO 2002010339 A2 20020207 WO 2001-US24469 20010801  
WO 2002010339 A3 20020404  
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GR, GE, GH,  
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, NO, NZ, PL, PT,  
RO, RU, SD, SE, SG, SI, SK, SL, TJ, TW, TR, TT, TZ, UA, UG, UZ,  
VN, YU, ZA, ZW, AM, AZ, BY, BG, BR, BY, BZ, CA, CH, CN, CY,  
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, LV, MA, MR, NE, SN, TD, TG  
AU 2001-102519 A 20010310  
US 2000-222162P P 20000802

L3 ANSWER 4 OF 33 CAPLUS COPYRIGHT 2003 ACS  
ACCESSION NUMBER:  
DOCUMENT NUMBER:  
TITLE:  
INVENTOR(S) :  
PATENT ASSIGNEE(S) :  
SOURCE:  
DOCUMENT TYPE:  
LANGUAGE:  
FAMILY ACC. NUM. COUNT:  
PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE  
JP 2002355079 A2 20021210 JP 2002-69354 20020313  
JP 2001-73183 A 20010314  
JP 2001-74993 A 20010315  
JP 2001-102519 A 20010310  
L3 ANSWER 5 OF 33 CAPLUS COPYRIGHT 2003 ACS  
ACCESSION NUMBER:  
TITLE:  
INVENTOR(S) :  
Tennan, David S., Pebble Beach, CA, UNITED STATES

PATENT INFORMATION:  
APPLICATION INFO.:  
US 2002177551 A1 20021128  
US 2001-870759 A1 20010510 (9)  
NUMBER DATE  
US 2000-208128P 20000531 (60)  
UTILITY APPLICATION

LEGAL REPRESENTATIVE: David S. Terman, P.O. Box 987, Pebble Beach, CA, 93953  
NUMBER OF CLAIMS: 30  
EXEMPLARY CLAIM: 1  
NUMBER OF DRAWINGS: 3 Drawing Page(s)  
LINE COUNT: 17323  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 6 OF 33 USPTATFUL  
ACCESSION NUMBER: 2002:259381 USPTATFUL  
TITLE: Materials and methods relating to lipid metabolism  
INVENTOR(S): Ballinger, Dennis G., Menlo Park, CA, UNITED STATES  
Loeb, Deborah, San Jose, CA, UNITED STATES  
Montgomery, Julie R., Santa Cruz, CA, UNITED STATES  
Tang, Y. Tom, San Jose, CA, UNITED STATES  
Zhou, Ping, Cupertino, CA, UNITED STATES  
Goodrich, Kyle, San Jose, CA, UNITED STATES  
Liu, Chenghua, San Jose, CA, UNITED STATES  
Asundi, Vinod, Foster City, CA, UNITED STATES  
Zhao, Qing A., San Jose, CA, UNITED STATES  
Wehrman, Tom, Stanford, CA, UNITED STATES  
Drananac, Radoje T., Palo Alto, CA, UNITED STATES  
Ren, Feiyan, Cupertino, CA, UNITED STATES  
Qian, Xiaohong B., San Jose, CA, UNITED STATES  
Mang, Dunxui, Poway, CA, UNITED STATES

PATENT INFORMATION: US 2002:422853 A1 2002:1003  
APPLICATION INFO.: US 2001-835996 A1 2001:0416 (9)  
RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2000-714936, filed on 17 Nov 2000, PENDING Continuation-in-part of Ser. No. US 2000-667298, filed on 22 Sep 2000, PENDING Continuation-in-part of Ser. No. US 2000-631451, filed on 3 Aug 2000, PENDING Continuation-in-part of Ser. No. US 2000-598042, filed on 20 Jun 2000, PENDING

NUMBER	KIND	DATE
US 2002:422853	A1	2002:1003
US 2001-835996	A1	2001:0416 (9)

PRIORITY INFORMATION: US 2000-197137P 2000:0414 (60)  
DOCUMENT TYPE: Utility  
FILE SEGMENT: APPLICATION  
LEGAL REPRESENTATIVE: MARSHALL, GERSTEIN & BORUN, 6300 SEARS TOWER, 233 SOUTH WACKER, CHICAGO, IL, 60606-6357  
NUMBER OF CLAIMS: 20  
EXEMPLARY CLAIM: 1  
NUMBER OF DRAWINGS: 30 Drawing Page(s)  
LINE COUNT: 9120  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 7 OF 33 USPTATFUL  
ACCESSION NUMBER: 2002:206116 USPTATFUL  
TITLE: Toxicant-induced differential gene expression  
INVENTOR(S): Reichman-Olson, John F., Montclair, NJ, UNITED STATES

NUMBER	KIND	DATE
US 2002:110808	A1	2002:0815
US 2000-489220	A1	2000:0121 (9)

UTILITY  
APPLICATION  
VICKI G. NORTON, ESQ., BROBECK, PHLEGER AND HARRISON LLP, 12390 EL COMINO REAL, SAN DIEGO, CA, 92130  
1  
7 Drawing Page(s)

LINE COUNT: 5161  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 8 OF 33 USPTATFUL  
ACCESSION NUMBER: 2002:164658 USPTATFUL  
TITLE: Immunotherapeutic methods for extracorporeal modulation of CD36 and its ligands  
INVENTOR(S): Srivastava, Pramod K., Avon, CT, UNITED STATES

NUMBER	KIND	DATE
US 2002:086276	A1	2002:0704
US 2000-750973	A1	2000:1228 (9)

UTILITY  
APPLICATION  
PENNIE AND EDMONDS, 1155 AVENUE OF THE AMERICAS, NEW YORK, NY, 100362711

NUMBER OF CLAIMS: 1813  
EXEMPLARY CLAIM: 1  
LINE COUNT: 1813  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 9 OF 33 USPTATFUL  
ACCESSION NUMBER: 2002:66639 USPTATFUL  
TITLE: Compositions comprising heat shock proteins or alpha(2) macroglobulin, antigenic molecules and saponins, and methods of use thereof  
INVENTOR(S): Armen, Garo H., Manhasac, NY, UNITED STATES

NUMBER	KIND	DATE
US 2002:037290	A1	2002:0328
US 2001-909778	A1	2001:0720 (9)

PATENT INFORMATION: US 2000-223133P 2000:0807 (60)  
APPLICATION INFO.: Utility  
RELATED APPLN. INFO.: Application  
LEGAL REPRESENTATIVE: Pennie & Edmonds LLP, 1155 Avenue of the Americas, New York, NY, 10036-2711  
NUMBER OF CLAIMS: 119  
EXEMPLARY CLAIM: 1  
LINE COUNT: 4136  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 10 OF 33 USPTATFUL  
ACCESSION NUMBER: 2002:48016 USPTATFUL  
TITLE: Complexes of alpha (2) macroglobulin and antigenic molecules for immunotherapy  
INVENTOR(S): Srivastava, Pramod K., Avon, CT, UNITED STATES

NUMBER	KIND	DATE
US 2002:028207	A1	2002:0107
US 2001-873403	A1	2001:0604 (9)

UTILITY  
APPLICATION  
Continuation-in-part of Ser. No. US 2000-625139, filed on 25 Jul 2000, PENDING

PATENT INFORMATION: US 2000-209266P 2000:0602 (60)  
APPLICATION INFO.: Utility  
RELATED APPLN. INFO.: Application  
LEGAL REPRESENTATIVE: Pennie and Edmonds, 1155 Avenue of the Americas, New

YORK, NY, 100362711

NUMBER OF CLAIMS: 36  
EXEMPLARY CLAIM: 1  
NUMBER OF DRAWINGS: 65 Drawing Page(s)  
LINE COUNT: 4477  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 11 OF 33 USPATFUL  
ACCESSION NUMBER: 2002:297296 USPATFUL  
TITLE: Methods for inhibition of membrane fusion-associated events, including respiratory syncytial virus transmission  
INVENTOR(S): Bolognesi, Dani Paul, Durham, NC, United States  
Matthews, Thomas James, Durham, NC, United States  
Wild, Carl T., Durham, NC, United States  
Barney, Shawn O'Lin, Cary, NC, United States  
Lambert, Dennis Michael, Cary, NC, United States  
Petteaway, Stephen Robert, Cary, NC, United States  
Langlois, Alphonse J., Durham, NC, United States  
Trimeris, Inc., Durham, NC, United States (U.S. corporation)

PATENT ASSIGNEE(S):

PATENT INFORMATION:  
APPLICATION INFO: US 6479055 B1 20021112  
RELATED APPL. INFO: US 1995-470896 19950606 (8)  
Continuation-in-part of Ser. No. US 1994-360107, filed on 20 Dec 1994, now patented, Pat. No. US 6017536  
Continuation-in-part of Ser. No. US 1994-255208, filed on 7 Jun 1994  
Continuation-in-part of Ser. No. US 1993-73028, filed on 7 Jun 1993, now patented, Pat. No. US 5464933  
UTILITY GRANTED

DOCUMENT TYPE:  
FILE SEGMENT:  
LEGAL REPRESENTATIVE: Stucker, Jeffrey  
Feminie & Edmonds LLP  
NUMBER OF CLAIMS: 44  
EXEMPLARY CLAIM: 1  
NUMBER OF DRAWINGS: 84 Drawing Figure(s); 83 Drawing Page(s)  
LINE COUNT: 26553  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 12 OF 33 USPATFUL  
ACCESSION NUMBER: 2002:136555 USPATFUL  
TITLE: Methods of modulating an immune response to antigen, and cells for use in the method  
INVENTOR(S): Segal, Andrew H., Boston, MA, United States  
PATENT ASSIGNEE(S): Whitehead Institute for Biomedical Research, Cambridge, MA, United States (U.S. corporation)

NUMBER	KIND	DATE
US 6403080	B1	20020611
US 1999-339523		19990624 (9)
Division of Ser. No. US 1997-826259, filed on 27 Mar 1997, now patented, Pat. No. US 5951976		
NUMBER	DATE	
US 1996-14364P	19960328 (60)	

PRIORITY INFORMATION:  
DOCUMENT TYPE: UTILITY  
FILE SEGMENT: GRANTED  
PRIMARY EXAMINER: Bansal, Geetha P.  
LEGAL REPRESENTATIVE: Williams, Kathleen Madden, Palmer & Dodge, LLP  
NUMBER OF CLAIMS: 25

EXEMPLARY CLAIM: 1  
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)  
LINE COUNT: 2153  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 13 OF 33 CAPLUS COPYRIGHT 2003 ACS  
ACCESSION NUMBER: 2002:471412 CAPLUS  
TITLE: The endoplasmic reticulum-resident heat shock protein Grp96 activates dendritic cells via the toll-like receptor 2/4 pathway  
AUTHOR(S): Vabulas, Ramunas M.; Braedel, Sibylla; Hile, Norbert; Singh-Jasuja, Harpreet; Hertter, Sylvia; Ahmad-Nejad, Parviz; Kirschning, Carsten J.; da Costa, Clarissa; Ramnasee, Hans-Georg; Wagner, Hermann; Schild, Hansjorg  
INSTITUTE FOR MEDICAL MICROBIOLOGY, IMMUNOLOGY AND HYGIENE, TECHNICAL UNIVERSITY OF MUNICH, MUNICH, D-81675, GERMANY  
JOURNAL OF BIOLOGICAL CHEMISTRY (2002), 277(23), 20847-20853  
CODEN: JBCHA3; ISSN: 0021-9258  
AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY  
JOURNAL  
English

SOURCE: 35  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

PUBLISHER:  
DOCUMENT TYPE:  
LANGUAGE:  
REFERENCE COUNT:

L3 ANSWER 14 OF 33 CAPLUS COPYRIGHT 2003 ACS  
ACCESSION NUMBER: 2002:899128 CAPLUS  
TITLE: Structure-function studies of the receptors for complement C1q  
AUTHOR(S): McCreath, E.; Gaege, P.  
CORPORATE SOURCE: University of Oxford, Sir William Dunn School of Pathology, Oxford, OX1 3RE, UK  
SOURCE: Biochemical Society Transactions (2002), 30(6), 1010-1014  
CODEN: BCBSTB; ISSN: 0300-5127  
Portland Press Ltd.  
JOURNAL: General Review  
English

PUBLISHER:  
DOCUMENT TYPE:  
LANGUAGE:  
REFERENCE COUNT:

L3 ANSWER 15 OF 33 MEDLINE MEDLINE  
ACCESSION NUMBER: 2002051981  
DOCUMENT NUMBER: 21636470 PubMed ID: 11777948  
TITLE: The receptor for heat shock protein 60 on macrophages is saturable, specific, and distinct from receptors for other heat shock proteins.  
AUTHOR: Habich-Christiane; Baumgart Karina; Kolb Hubert; Burkart Volker  
CORPORATE SOURCE: German Diabetes Research Institute at the Heinrich-Heine-University of Dusseldorf, Dusseldorf, Germany..  
SOURCE: JOURNAL OF IMMUNOLOGY, (2002 Jan 15) 168 (2) 569-76.  
JOURNAL CODE: 2985117R. ISSN: 0022-1767.  
United States  
JOURNAL: Article: (JOURNAL ARTICLE)  
English  
Abridged Index Medicus Journals, Priority Journals  
200201



INVENTOR(S) : modulation of T helper-1 and T helper-2 cells and diseases associated therewith  
Hanshan, Catherine F.; Feldman, Marc; Trepelchto, William L.  
PATENT ASSIGNEE(S) : Genetics Institute, Inc., USA; Kennedy Institute of Rheumatology  
PCT Int. Appl., 115 pp.  
SOURCE :  
DOCUMENT TYPE : Patent  
LANGUAGE : English  
FAMILY ACC. NUM. COUNT : 1  
PATENT INFORMATION :  
CODEN: PIXXD2

PATENT NO. : 2001088199  
KIND : A2  
DATE : 20011122  
APPLICATION NO. : 2001-0516022  
DATE : 20010517  
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, LU, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NZ, NI, NO, NU, OI, PA, PE, PG, PH, PK, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, GM, KE, LS, MM, MW, MZ, SD, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GN, GW, ML, MR, NE, SN, TD, TG  
PRIORITY APPL. INFO.: A1 20020404 US 2001-860655 20010517  
US 2002039734 US 2000-205204P P 20000518

L3 ANSWER 21 OF 33 CAPLUS COPYRIGHT 2003 ACS  
ACCESSION NUMBER: 2001.676999 CAPLUS  
DOCUMENT NUMBER: 135:252790  
TITLE: Single nucleotide polymorphisms in human genes  
INVENTOR(S): Cargill, Michele; Ireland, James S.; Lander, Eric S.  
PATENT ASSIGNEE(S): Whitehead Institute for Biomedical Research, USA  
SOURCE: PCT Int. Appl., 145 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO. : 2001066800  
KIND : A2  
DATE : 20010913  
APPLICATION NO. : 2001-0517268  
DATE : 20010307  
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NZ, NI, NO, NU, OI, PA, PE, PG, PH, PK, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, GM, KE, LS, MM, MW, MZ, SD, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GN, GW, ML, MR, NE, SN, TD, TG  
PRIORITY APPL. INFO.: A1 20020314 US 2001-801274 20010307  
US 2000-187510P P 20000307  
US 2000-206129P P 20000522

L3 ANSWER 22 OF 33 CAPLUS COPYRIGHT 2003 ACS  
ACCESSION NUMBER: 2001.319729 CAPLUS  
DOCUMENT NUMBER: 134:320865  
TITLE: Regulation of apob for diagnosis, treatment and drug screening for cardiovascular and metabolic disorders or syndromes  
INVENTOR(S): Fisher, Edward A.; Williams, Kevin Jon  
PATENT ASSIGNEE(S): Thomas Jefferson University, USA

SOURCE: PCT Int. Appl., 59 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO. : 2001030354  
KIND : A1  
DATE : 20010503  
APPLICATION NO. : 2000-US29699  
DATE : 20001026  
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NZ, NI, NO, NU, OI, PA, PE, PG, PH, PK, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, GM, KE, LS, MM, MW, MZ, SD, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GN, GW, ML, MR, NE, SN, TD, TG  
PRIORITY APPL. INFO.: 1 US 1999-161537P P 19991026  
REFERENCE COUNT: 1  
THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 23 OF 33 CAPLUS COPYRIGHT 2003 ACS  
ACCESSION NUMBER: 2001.67794 CAPLUS  
DOCUMENT NUMBER: 135:252790  
TITLE: Human respiratory syncytial virus peptides with anti-infective and antiviral activities  
INVENTOR(S): Barney, Shawn O.; Lin, Cary, NC, United States  
PATENT ASSIGNEE(S): Lambert, Dennis Michael, Cary, NC, United States  
Pettey, Stephen Robert, Cary, NC, United States  
Trimeris, Inc., Durham, NC, United States (U.S. corporation)

PATENT INFORMATION: US 6228983 B1 20010508  
APPLICATION INFO.: US 1995-485264 19950607 (b)  
RELATED APPL. INFO.: Division of Ser. No. US 1995-470896, filed on 6 Jun 1995 Continuation-in-part of Ser. No. US 1994-360107, filed on 20 Dec 1994 Continuation-in-part of Ser. No. US 1994-255208, filed on 7 Jun 1994  
Continuation-in-part of Ser. No. US 1993-73028, filed on 7 Jun 1993, now patented, Pat. No. US 5464933

DOCUMENT TYPE: Utility  
FILE SEGMENT: Granted  
PRIMARY EXAMINER: Scheiner, Laurie  
ASSISTANT EXAMINER: Parkin, Jeffrey S.  
LEGAL REPRESENTATIVE: Penne & Edmonds LLP  
NUMBER OF CLAIMS: 62  
EXEMPLARY CLAIMS: 1  
NUMBER OF DRAWINGS: 84 Drawing Figure(s); 83 Drawing Page(s)  
LINE COUNT: 32166  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 24 OF 33 CAPLUS COPYRIGHT 2003 ACS  
ACCESSION NUMBER: 2001.286503 CAPLUS  
DOCUMENT NUMBER: 135:136110  
TITLE: Adjuvanticity of .alpha.2-macroglobulin, an independent ligand for the heat shock protein receptor CD91  
BINDER, Robert J.; Karimeddini, David; Srivastava, Pramod K.  
AUTHOR(S): Center for Immunotherapy of Cancer and Infectious Diseases, University of Connecticut School of Medicine, Farmington, CT, 06030, USA  
CORPORATE SOURCE:

SOURCE: Journal of Immunology (2001), 166(8), 4968-4972  
 PUBLISHER: JOMIAJ; ISSN: 0022-1767  
 DOCUMENT TYPE: American Association of Immunologists  
 LANGUAGE: Journal  
 REFERENCE COUNT: 14  
 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 25 OF 33 CAPLUS COPYRIGHT 2003 ACS  
 ACCESSION NUMBER: 2001:782994 CAPLUS  
 DOCUMENT NUMBER: 136:68297  
 TITLE: To find the road traveled to tumor immunity: the trafficking itineraries of molecular chapones in antigen-presenting cells  
 AUTHOR(S): Berwin, B.; Nicchitta, C. V.  
 CORPORATE SOURCE: Department of Cell Biology, Duke University Medical Center, Durham, NC, 27710, USA  
 SOURCE: Traffic (Copenhagen, Denmark) (2001), 2(10), 690-697  
 PUBLISHER: TRAFPA; ISSN: 1398-9219  
 DOCUMENT TYPE: Munksgaard International Publishers Ltd.  
 LANGUAGE: Journal; General Review  
 REFERENCE COUNT: 41  
 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 26 OF 33 CAPLUS COPYRIGHT 2003 ACS  
 ACCESSION NUMBER: 2001:263289 CAPLUS  
 DOCUMENT NUMBER: 135:32507  
 TITLE: CD91 is a common receptor for heat shock proteins gp96, hsp90, hsp70, and calreticulin  
 AUTHOR(S): Basu, Sreyashi; Binder, Robert J.; Ramalingam, Thirumalai; Srivastava, Pramod K.  
 CORPORATE SOURCE: Center for Immunotherapy of Cancer and Infectious Diseases, University of Connecticut School of Medicine, Farmington, CT, 06030, USA  
 SOURCE: Immunity (2001), 14(3), 303-313  
 PUBLISHER: IMMUN; ISSN: 1074-7613  
 DOCUMENT TYPE: Cell Press  
 LANGUAGE: Journal  
 REFERENCE COUNT: 34  
 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 27 OF 33 CAPLUS COPYRIGHT 2003 ACS  
 ACCESSION NUMBER: 2001:361126 CAPLUS  
 DOCUMENT NUMBER: 135:150447  
 TITLE: Differential expression of multiple genes during articular chondrocyte redifferentiation  
 AUTHOR(S): Haudenschild, Dominik R.; McPherson, John M.; Tubo, Ross; Binette, Francois  
 CORPORATE SOURCE: Genzyme Tissue Repair, Framingham, MA, USA  
 SOURCE: Anatomical Record (2001), 263(1), 91-98  
 PUBLISHER: ANREK; ISSN: 0003-276X  
 DOCUMENT TYPE: Wiley-Liss, Inc.  
 LANGUAGE: Journal  
 REFERENCE COUNT: 36  
 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 28 OF 33 CAPLUS COPYRIGHT 2003 ACS  
 ACCESSION NUMBER: 2000:759895 CAPLUS  
 DOCUMENT NUMBER: 134:28172  
 TITLE: The expression of adipogenic genes is decreased in obesity and diabetes mellitus

AUTHOR(S): Nadler, Samuel T.; Stoeck, Jonathan P.; Schueler, Kathryn L.; Tanimoto, Gene; Yandell, Brian S.; Attie, Alan D.  
 CORPORATE SOURCE: Department of Biochemistry, University of Wisconsin, Madison, WI, 53706, USA  
 SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2000), 97(21), 11371-11376  
 PUBLISHER: PNAS; ISSN: 0027-8424  
 DOCUMENT TYPE: National Academy of Sciences  
 LANGUAGE: Journal  
 REFERENCE COUNT: 40  
 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 29 OF 33 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2000:908423 CAPLUS  
 DOCUMENT NUMBER: 134:203644  
 TITLE: Morphologic analysis correlates with gene expression changes in cultured F344 rat mesothelial cells  
 AUTHOR(S): Crosby, L. M.; Hyder, K. S.; DeAngelis, A. B.; Keppler, T. B.; Gaskill, B.; Benavides, G. R.; Yoon, L.; Morgan, K. T.  
 CORPORATE SOURCE: University of North Carolina at Chapel Hill, Curriculum in Toxicology/U.S. EPA NHEERL, Research Triangle Park, NC, 27711, USA  
 SOURCE: Toxicology and Applied Pharmacology (2000), 169(3), 205-221  
 PUBLISHER: TXAP; ISSN: 0041-008X  
 DOCUMENT TYPE: Academic Press  
 LANGUAGE: Journal  
 REFERENCE COUNT: 60  
 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 30 OF 33 MEDLINE MEDLINE  
 ACCESSION NUMBER: 2001216038  
 DOCUMENT NUMBER: 21205395  
 TITLE: CD91: a receptor for heat shock protein gp96.  
 COMMENT: Comment in: Nat Immunol. 2000 Aug;1(2):100-1  
 AUTHOR: Binder R J; Han D K; Srivastava P K  
 CORPORATE SOURCE: Center for Immunotherapy of Cancer and Infectious Diseases, University of Connecticut School of Medicine, Farmington, CT 06030, USA.  
 CONTRACT NUMBER: CA64394 (NCI)  
 SOURCE: Nat Immunol. (2000 Aug) 1 (2) 151-5.  
 PUB. COUNTRY: Journal code: 10941354. ISSN: 1529-2908.  
 DOCUMENT TYPE: United States  
 LANGUAGE: Journal; Article: (JOURNAL ARTICLE)  
 FILE SEGMENT: English  
 ENTRY MONTH: Priority Journals  
 ENTRY DATE: 200105  
 Entered STM: 20010521  
 Last Updated on STM: 20010521  
 Entered Medline: 20010517

L3 ANSWER 31 OF 33 CAPLUS COPYRIGHT 2003 ACS  
 ACCESSION NUMBER: 1999:795994 CAPLUS  
 DOCUMENT NUMBER: 132:31744  
 TITLE: Gene probes used for genetic profiling in healthcare screening and planning  
 INVENTOR(S): Roberts, Gareth Wyn  
 PATENT ASSIGNEE(S): Genosic Pharma Ltd., UK  
 SOURCE: PCT Int. Appl., 745 pp.





L3 ANSWER 12 OF 33 USPATFULL  
SUMM  
TABLE 1  
Exemplary Opsonin, APC binding moiety/APC receptor pairs useful according to the invention.  
Exemplary APC Binding  
Opsonin Moiety Receptor  
.alpha.-2 macroglobulin Val(1299)-Ala(1451) of  
human .alpha.-2 m receptor  
C3b 42 N-terminal amino acids CRI  
of the .alpha.' chain of human  
C3b  
SUMM  
. . . . . bacilli bacterial antigens such as lipopolysaccharides and other gram-negative bacterial antigen components; Mycobacterium tuberculosis bacterial antigens such as mycolic acid, heat shock protein 65 (HSP65), the 30kDa major secreted protein, antigen 85A and other mycobacterial antigen components; Helicobacter pylori bacterial antigen components; pneumococcal . . . . . and methods of the invention include, but are not limited to, candida fungal antigen components; histoplasma fungal antigens such as heat shock protein 60 (HSP60) and other . . . . . histoplasma fungal antigen components; cryptococcal fungal antigens such as capsular polysaccharides and other cryptococcal fungal antigen. . . . .

SUMM  
=> his  
HIS IS NOT A RECOGNIZED COMMAND  
The previous command name entered was not recognized by the system.  
For a list of commands available to you in the current file, enter  
"HELP COMMANDS" at an arrow prompt (=>).

=> d his  
(FILE 'HOME' ENTERED AT 15:25:49 ON 20 FEB 2003)  
FILE 'MEDLINE, CANCERLIT, BIOSIS, CONFSCI, EMBASE, CAPLUS, USPATFULL'  
ENTERED AT 15:26:27 ON 20 FEB 2003  
L1 72563 S HEAT (A) SHOCK (A) PROTEIN  
L2 40 S L1 AND ALPHA (A) 2 (A) MACROGLOBULIN (A) RECEPTOR  
L3 33 DUP REM L2 (7 DUPLICATES REMOVED)  
=> s l1 and antibody?  
L4 12721 L1 AND ANTIBOD?  
=> s l4 abd l2  
MISSING OPERATOR L4 ABD  
The search profile that was entered contains terms or nested terms that are not separated by a logical operator.  
L5 => s l4 and l2  
21 L4 AND L2  
=> dup rem l5  
PROCESSING COMPLETED FOR L5  
L6 19 DUP REM L5 (2 DUPLICATES REMOVED)  
=> d 1-19

L6 ANSWER 1 OF 19 USPATFULL  
AN 2003:40533 USPATFULL  
TI Methods for the inhibition of Epstein-Barr virus transmission employing

IN anti-viral peptides capable of abrogating viral fusion and transmission  
Barney, Shawn O'lin, Cary, NC, United States  
Lambert, Dennis Michael, Cary, NC, United States  
Petreway, Stephen Robert, Cary, NC, United States  
Patterson, Inc., Durham, NC, United States (U.S. corporation)  
PA 6516013 B1 20030211  
PI US 1995-485546  
RI Continuation-in-part of Ser. No. US 1994-360107, filed on 20 Dec 1994, now patented, Pat. No. US 6017536 Continuation-in-part of Ser. No. US 1994-255208, filed on 7 Jun 1994 Continuation-in-part of Ser. No. US 1993-73028, filed on 7 Jun 1993, now patented, Pat. No. US 5464933  
DT Utility  
FS GRANTED  
LN CNT 24700  
INCL INCLM: 435/005.000  
INCLM: 424/230.100; 530/300.000; 530/324.000; 530/325.000; 530/326.000  
NCL NCLM: 435/005.000  
NCLM: 424/230.100; 530/300.000; 530/324.000; 530/325.000; 530/326.000  
IC ICM: C12Q001-70  
EXF 435/5; 530/300; 530/324-329; 530/350; 424/230.1  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2003 ACS  
AN 2002:937303 CAPLUS  
DN 138:20443  
TI Endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes  
IN Kondo, Akhiro, Takeda, Takeshi; Mizutani, Shigetoshi; Tajiimoto, Yoshimasa; Takashima, Ryokichi; Enoki, Yuki; Kato, Ikunoshin  
PA Takara Bio Inc., Japan  
SO Jpn. Kokai Tokyo Koho, 386 pp.  
DT Patent  
LA Japanese  
FAN CNT 1  
PATENT NO. KIND DATE APPLICATION NO. DATE  
PI JP 2002355079 A2 20021210 JP 2002-69354 20020313  
PRAI JP 2001-73183 A 20010314  
JP 2001-74993 A 20010315  
JP 2001-102519 A 20010330

L6 ANSWER 3 OF 19 USPATFULL  
AN 2002:335069 USPATFULL  
TI Compositions and methods for treatment of neoplastic disease  
IN Terman, David S., Reddie Beach, CA, UNITED STATES  
PI US 2002177551 A1 20021128  
AI US 2001-870759 A1 20010530 (9)  
PRAI US 2000-208128P 20000531 (60)  
DT Utility  
FS APPLICATION  
LN CNT 17323  
INCL INCLM: 514/012.000  
INCLM: 435/325.000; 530/350.000  
NCL NCLM: 514/012.000  
NCLM: 435/325.000; 530/350.000  
IC ICM: A61K038-17  
ICS: C12N005-06; C07K014-705  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 4 OF 19 USPATFULL  
AN 2002:259381 USPATFULL  
TI Materials and methods relating to lipid metabolism

IN Ballinger, Dennis G., Menlo Park, CA, UNITED STATES  
 Loeb, Deborah, San Jose, CA, UNITED STATES  
 Montgomery, Julie R., Santa Cruz, CA, UNITED STATES  
 Tang, Y. Tom, San Jose, CA, UNITED STATES  
 Zhou, Ping, Cupertino, CA, UNITED STATES  
 Goodrich, Ryle, San Jose, CA, UNITED STATES  
 Liu, Chenghua, San Jose, CA, UNITED STATES  
 Asundi, Vinod, Foster City, CA, UNITED STATES  
 Zhao, Qing A., San Jose, CA, UNITED STATES  
 Wehman, Tom, Stanford, CA, UNITED STATES  
 Drmanac, Radolje T., Palo Alto, CA, UNITED STATES  
 Ren, Feiyan, Cupertino, CA, UNITED STATES  
 Qian, Xiaohong B., San Jose, CA, UNITED STATES  
 Wang, Dunrui, Poway, CA, UNITED STATES  
 PI US 2002142953 AI 20021003  
 US 2001-83596 AI 20010416 (9)  
 RLI Continuation-in-part of Ser. No. US 2000-714936, filed on 17 Nov 2000,  
 PENDING Continuation-in-part of Ser. No. US 2000-667296, filed on 22 Sep  
 2000, PENDING Continuation-in-part of Ser. No. US 2000-631451, filed on  
 3 Aug 2000, PENDING Continuation-in-part of Ser. No. US 2000-558042,  
 filed on 20 Jun 2000, PENDING  
 PRAI US 2000-197137P 20000414 (60)  
 DT Utility  
 FS APPLICATION  
 LN.CNT 9120  
 INCL INCLM: 514/012.000  
 INCLS: 435/069.100; 435/325.000; 435/320.100; 530/359.000; 435/196.000;  
 NCLM: 514/012.000  
 NCL: 435/069.100; 435/325.000; 435/320.100; 530/359.000; 435/196.000;  
 IC [7]  
 ICM: A61K038-17  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 L6 ANSWER 5 OF 19 USPTAFULL  
 AN 2002:206116 USPTAFULL  
 TI Toxicant-induced differential gene expression  
 IN Reichart-Olson, John F., Montclair, NJ, UNITED STATES  
 PI US 2002110808 AI 20020815  
 DT US 2000-489220 AI 20000121 (9)  
 FS Utility  
 FS APPLICATION  
 LN.CNT 5161  
 INCL INCLM: 435/006.000  
 INCLS: 435/091.200; 536/023.100  
 NCLM: 435/006.000  
 NCL: 435/091.200; 536/023.100  
 IC [7]  
 ICM: C120001-68  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 L6 ANSWER 6 OF 19 USPTAFULL  
 AN 2002:164658 USPTAFULL  
 TI Immunotherapeutic methods for extracorporeal modulation of CD36 and its  
 ligands  
 IN Sriastava, Pramod K., Avon, CT, UNITED STATES  
 PI US 2002086276 AI 20020704  
 DT US 2000-750973 AI 20001228 (9)  
 FS Utility  
 FS APPLICATION  
 LN.CNT 1813  
 INCL INCLM: 435/002.000

NCL INCLS: 424/140.100  
 NCLM: 435/002.000  
 NCLS: 424/140.100  
 IC [7]  
 ICM: A61K039-395  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 L6 ANSWER 7 OF 19 USPTAFULL  
 AN 2002:66639 USPTAFULL  
 TI Compositions comprising heat shock proteins  
 or alpha(2) macroglobulin, antigenic molecules and saponins, and methods  
 of use thereof  
 IN Armen, Garo H., Manhasset, NY, UNITED STATES  
 PI US 2002037290 AI 20020328  
 DT US 2001-909778 AI 20010720 (9)  
 PRAI US 2000-223133P 20000807 (60)  
 FS Utility  
 FS APPLICATION  
 LN.CNT 4136  
 INCL INCLM: 424/178.100  
 INCLS: 514/012.000; 514/026.000  
 NCLM: 424/178.100  
 NCL: 424/178.100  
 IC [7]  
 ICM: A61K039-395  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 L6 ANSWER 8 OF 19 USPTAFULL  
 AN 2002:48016 USPTAFULL  
 TI Complexes of alpha (2) macroglobulin and antigenic molecules for  
 immunotherapy  
 IN Srivastava, Pramod K., Avon, CT, UNITED STATES  
 PI US 2002028207 AI 20020307  
 DT US 2001-873403 AI 20010604 (9)  
 RLI Continuation-in-part of Ser. No. US 2000-625139, filed on 25 Jul 2000,  
 PENDING  
 PRAI US 2000-209266P 20000602 (60)  
 DT Utility  
 FS APPLICATION  
 LN.CNT 4477  
 INCL INCLM: 424/185.100  
 INCLS: 424/190.100; 424/178.100; 530/391.100  
 NCLM: 424/185.100  
 NCL: 424/190.100; 424/178.100; 530/391.100  
 IC [7]  
 ICM: A61K039-40  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 L6 ANSWER 9 OF 19 USPTAFULL  
 AN 2002:297296 USPTAFULL  
 TI Methods for inhibition of membrane fusion-associated events, including  
 respiratory syncytial virus transmission  
 IN Bolognesi, Dani Paul, Durham, NC, United States  
 Matthews, Thomas James, Durham, NC, United States  
 Wild, Carl T., Durham, NC, United States  
 Barney, Shawn O'Lin, Cary, NC, United States  
 Lambert, Dennis Michael, Cary, NC, United States  
 Letteway, Stephen Robert, Cary, NC, United States  
 Langlois, Alphonse J., Durham, NC, United States  
 Trimeris, Inc., Durham, NC, United States (U.S. corporation)  
 PI US 6479055 BI 20021112  
 US 1995-470896 19950606 (8)  
 RLI Continuation-in-part of Ser. No. US 1994-360107, filed on 20 Dec 1994,

now patented, Pat. No. US 6017536 Continuation-in-part of Ser. No. US 1994-255208, filed on 7 Jun 1994 Continuation-in-part of Ser. No. US 1993-73028, filed on 7 Jun 1993, now patented, Pat. No. US 5464933

DT Utility

PS GRANTED

LN.CNT 26553

INCL INCLM: 424/211.100

NCL INCLM: 424/186.100; 530/324.000

NCLM: 424/211.100

NCLS: 424/186.100; 530/324.000

IC [7]

ICM: A61K039-145

EXF 435/5; 435/240.2; 424/184.1-189.1; 424/204.1-211.1; 424/225.1; 424/227.1; 424/230.1; 514/1; 514/2; 530/324; 530/350; 530/826

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 10 OF 19 USPATFULL

TI 2002:136555 USPATFULL

Methods of modulating an immune response to antigen, and cells for use in the method

IN Segal, Andrew H., Boston, MA, United States

PA Whitehead Institute for Biomedical Research, Cambridge, MA, United States (U.S. corporation)

PI US 6403080 B1 20020611

AI US 1999-339523 19990624 (9)

RLI Division of Ser. No. US 1997-826259, filed on 27 Mar 1997, now patented, Pat. No. US 5951976 19960328 (60)

PRAI US 1996-14364P

DT Utility

FS GRANTED

LN.CNT 2153

INCLM: 424/093.100

INCLS: 424/093.200; 424/093.210; 424/093.700; 424/093.710; 424/136.100; 435/325.000; 514/002.000; 514/012.000; 530/387.300

NCLM: 424/093.100

NCLS: 424/093.200; 424/093.210; 424/093.700; 424/093.710; 424/136.100; 435/325.000; 514/002.000; 514/012.000; 530/387.300

IC [7]

ICM: A01N063-00

EXF 1CS: A61K039-395; A61K038-00; C12P021-08

424/93.21; 424/93.7; 424/93.1; 424/93.2; 424/93.71; 424/136.1; 435/325; 514/12; 514/21; 530/387.3

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2003 ACS

AN 2002:899128 CAPLUS

DN 138:88135

TI Structure-function studies of the receptors for complement C1q

AU McGee, E.; Gaege, P.

CS University of Oxford, Sir William Dunn School of Pathology, Oxford, OX1 3RE, UK

SO Biochemical Society Transactions (2002), 30(6), 1010-1014

COBEN: BCSTB5; ISSN: 0300-5127

PB Portland Press Ltd.

DT Journal: General Review

LA English

RE.CNT 50

ALL CITATIONS AVAILABLE IN THE RE FORMAT

ALL CITATIONS AVAILABLE FOR THIS RECORD

L6 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2003 ACS

AN 2001:866449 CAPLUS

DN 136:36328

TI Alpha 2 macroglobulin receptors as a heat shock protein receptor and uses thereof

IN Srivastava, Pramod K.

PA University of Connecticut Health Center, USA

SO PCT Int. Appl., 236 pp.

CODEN: PIXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

PI WO 2001092474 A1 20011206 WO 2001-US18041 20010604

W: AU, CA, JP

RM: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR

PRAI US 2000-209095P P 20000602

US 2000-625137 A 20000725

US 2000-688724 A 20000922

US 2000-750972 A 20001228

RE.CNT 1

ALL CITATIONS AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2003 ACS

AN 2001:851435 CAPLUS

DN 136:1570

TI Compositions, kits, and methods for identification and modulation of T helper-1 and T helper-2 cells and diseases associated therewith

IN Hanahan, Catherine F.; Feldman, Marc; Trepicchio, William L.

PA Genetics Institute, Inc., USA; Kennedy Institute of Rheumatology

SO PCT Int. Appl., 115 pp.

CODEN: PIXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

PI WO 2001088199 A2 20011122 WO 2001-US16022 20010517

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BE, BY, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, ME, MG, MK, MN, MW, MX, MY, NZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TT, TZ, UA, UG, UZ, VA, YU, ZA, ZW, AM, AZ, BY, BG, KZ, MD, RU, TJ, TM

RM: CH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GW, GN, HT, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, ME, MG, MK, MN, MW, MX, MY, NZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TT, TZ, UA, UG, UZ, VA, YU, ZA, ZW, AM, AZ, BY, BG, KZ, MD, RU, TJ, TM

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GW, GN, HT, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, ME, MG, MK, MN, MW, MX, MY, NZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TT, TZ, UA, UG, UZ, VA, YU, ZA, ZW, AM, AZ, BY, BG, KZ, MD, RU, TJ, TM

US 2002039734 A1 20020404

US 2001-86055 20010517

PRAI US 2000-205204P P 20000518

L6 ANSWER 14 OF 19 USPATFULL

AN 2001:67794 USPATFULL

TI Human respiratory syncytial virus peptides with antifusogenic and antiviral activities

IN Barney, Shawn O'Lin, Cary, NC, United States

PA Lambert, Dennis Michael, Cary, NC, United States

PTeraway, Stephen Robert, Cary, NC, United States

Triimeris, Inc., Durham, NC, United States (U.S. corporation)

PI US 6228983 B1 20010508

US 1993-485264 19950607 (8)

AI US 1993-485264

RLI Division of Ser. No. US 1995-470896, filed on 6 Jun 1995

Continuation-in-part of Ser. No. US 1994-360107, filed on 20 Dec 1994

Continuation-in-part of Ser. No. US 1994-255208, filed on 7 Jun 1994

Continuation-in-part of Ser. No. US 1993-73028, filed on 7 Jun 1993, now patented, Pat. No. US 5464933

DT Utility

FS Granted

LN.CNT 32166

[illegible]

TI	Regulation of apob for diagnosis treatment and drug screening for cardiovascular and metabolic disorders or syndromes
IN	Fisher, Edward A.; Williams, Kevin Jon
PA	Thomas Jefferson University, USA
SO	PCT Int. Appl., 59 pp.
	CODEN: PIXXD2
DT	Patent
LA	English
FA	PAN CNT 1
	PATENT NO.                      KIND      DATE                      APPLICATION NO.      DATE
PI	WO 2001030354                      A1      20010503                      WO 2000-052969      20001026
	W: AE, AC, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, DE, DG, DM, DK, DR, DT, DU, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MX, MY, NZ, OL, PA, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
	FW: GE, GH, KE, LS, MM, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, NO, PT, SE, BF, BJ, CF, CG, CI, CM, CA, GN, GW, ML, MR, NE, SN, TD, TG
PRAI	US 1999-161537P                      P      19991026
RE CNT	1                      THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
	ALL CITATIONS AVAILABLE IN THE RE FORMAT
L8	ANSWER 3 OF 4      USPATFUL
AN	2002:315069      USPATFUL
TI	Compositions and methods for treatment of neoplastic disease
IN	Terman, David S., Pebble Beach, CA, UNITED STATES
PI	US 2002177551                      A1      20021128
PRAI	US 2000-208128P                      20000531 (60)
DT	Utility
FS	APPLICATION
LN CNT	17323
INCL	INCLM: 514/012.000
	INCLS: 435/325.000; 530/350.000
NCL	NCLM: 514/012.000
	NCLS: 435/325.000; 530/350.000
IC	[7]
	ICH: A61K038-17
	ICS: C12N005-06; C07K014-705
	CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L8	ANSWER 4 OF 4      USPATFUL
AN	2002:259381      USPATFUL
TI	Materials and methods relating to lipid metabolism
IN	Hallinger, Dennis G., Menlo Park, CA, UNITED STATES
	Loeb, Deborah, San Jose, CA, UNITED STATES
	Montgomery, Julie R., Santa Cruz, CA, UNITED STATES
	Tang, Y. Tom, San Jose, CA, UNITED STATES
	Zhou, Ping, Cupertino, CA, UNITED STATES
	Goodrich, Rylee, San Jose, CA, UNITED STATES
	Li, Chenghua, San Jose, CA, UNITED STATES
	Ausudi, Vinod, Foster City, CA, UNITED STATES
	Zhao, Qing A., San Jose, CA, UNITED STATES
	Wehrman, Tom, Stanford, CA, UNITED STATES
	Dzmanac, Radoje T., Palo Alto, CA, UNITED STATES
	Ren, Peiyuan, Cupertino, CA, UNITED STATES
	Qian, Xiaohong B., San Jose, CA, UNITED STATES
	Wang, Dunru, Poway, CA, UNITED STATES
PI	US 2002142953                      A1      20021003
US	2002142953                      A1      20010416 (9)
US	2001-835996
US	2000-714936, filed on 17 Nov 2000,
PENDING	Continuation-in-part of Ser. No. US 2000-667298, filed on 22 Sep.

2000, PENDING Continuation-in-part of Ser. No. US 2000-631451, filed on 3 Aug 2000, PENDING Continuation-in-part of Ser. No. US 2000-598042, filed on 20 Jun 2000, PENDING

PRAI US 2000-197137P 20000414 (60)

DT Utility

FS APPLICATION

LN.CNT 9120

INCL INCLM: 514/012.000

INCLS: 435/069.100; 435/325.000; 435/320.100; 530/359.000; 435/196.000;

NCL INCLM: 514/012.000

NCLS: 435/069.100; 435/325.000; 435/320.100; 530/359.000; 435/196.000;

IC [7]

ICM: A61K038-17

ICS: C07H021-04; C12N009-16; C12P021-02; C12N005-06; C07K014-775

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d his

(FILE 'HOME' ENTERED AT 15:25:49 ON 20 FEB 2003)

FILE 'MEDLINE, CANCERLIT, BIOSIS, CONFSCI, EMBASE, CAPLUS, USPATFULL' ENTERED AT 15:26:27 ON 20 FEB 2003

L1 72563 S HEAT (A) SHOCK (A) PROTEIN

L2 40 S L1 AND ALPHA (A) 2 (A) MACROGLOBULIN (A) RECEPTOR

L3 33 DUP REM L2 (7 DUPLICATES REMOVED)

L4 12721 S L1 AND ANTIBODY

L5 21 S L4 AND L2

L6 19 DUP REM L5 (2 DUPLICATES REMOVED)

L7 1585 S AGONIST? AND L1

L8 4 S L7 AND L2

=> s 11 and peptide?

L9 8637 L1 AND PEPTIDE?

=> s 19 and 12

L10 27 L9 AND L2

=> dup rem 110

PROCESSING COMPLETED FOR L10

L11 24 DUP REM L10 (3 DUPLICATES REMOVED)

=> s 111 and modulates?

L12 11 L11 AND MODULATE?

=> d 1-11

L12 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2003 ACS

AN 2001:886449 CAPLUS

DN 136:36328

TI Alpha 2 macroglobulin receptors as

a heat shock protein receptor and uses

thereof

IN Strivastava, Pramod K.

PA University of Connecticut Health Center, USA

SO PCT Int. Appl., 236 PP.

COEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

PI WO 2001092474 A1 20011206 WO 2001-US18041 20010604

W: AU, CA, JP  
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,  
PT, SE, TR

PRAI US 2000-209095P P 20000602

US 2000-625137 A 20000725

US 2000-668724 A 20000922

US 2000-750972 A 20001228

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALT CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 11 USPATFULL

AN 2003:40533 USPATFULL

TI Methods for the inhibition of Epstein-Barr virus transmission employing

anti-viral peptides capable of abrogating viral fusion and transmission

IN

Barney, Shawn O'Lin, Cary, NC, United States

Lambert, Dennis Michael, Cary, NC, United States

Peteway, Stephen Robert, Cary, NC, United States

Trimeris, Inc., Durham, NC, United States (U.S. corporation)

PI US 6518013 B1 20030211

AI US 1995-485546 19950607 (8)

Continuation-in-part of Ser. No. US 1994-360107, filed on 20 Dec 1994,

now patented, Pat. No. US 6017536 Continuation-in-part of Ser. No. US

1994-255208, filed on 7 Jun 1994 Continuation-in-part of Ser. No. US

1993-73028, filed on 7 Jun 1993, now patented, Pat. No. US 5464933

Utility

DT GRANTED

FS

LN.CNT 24700

INCL INCLM: 435/005.000

INCLS: 424/230.100; 530/300.000; 530/324.000; 530/325.000; 530/326.000

NCL INCLM: 435/005.000

NCLS: 424/230.100; 530/300.000; 530/324.000; 530/325.000; 530/326.000

IC [7]

ICM: C12N001-70

EXF 435/5; 530/300; 530/324-329; 530/350; 424/230.1

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 3 OF 11 USPATFULL

AN 2002:315069 USPATFULL

TI Compositions and methods for treatment of neoplastic disease

IN Terman, David S., Pebble Beach, CA, UNITED STATES

PI US 2002177551 A1 20021128

AI US 2001-870759 A1 20010530 (9)

PRAI US 2000-208128P 20000531 (60)

Utility

FS APPLICATION

LN.CNT 17323

INCL INCLM: 514/012.000

INCLS: 435/325.000; 530/350.000

NCL INCLM: 514/012.000

NCLS: 435/325.000; 530/350.000

IC [7]

ICM: A61K038-17

ICS: C12N005-06; C07K014-705

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 4 OF 11 USPATFULL

AN 2002:297296 USPATFULL

TI Methods for inhibition of membrane fusion-associated events, including

respiratory syncytial virus transmission

Bolognesi, Dani Paul, Durham, NC, United States

Mathews, Thomas James, Durham, NC, United States

Wild, Carl T., Durham, NC, United States

Barney, Shawn O'Lin, Cary, NC, United States

Lambert, Dennis Michael, Cary, NC, United States

Peteway, Stephen Robert, Cary, NC, United States

PA Langlois, Alphonse J., Durham, NC, United States  
 PI Trimeris, Inc., Durham, NC, United States (U.S. corporation)  
 AI US 6479055 B1 20021112  
 INCL INCLM: 424/211.100  
 NCLM: 424/186.100; 530/324.000  
 NCLM: 424/211.100  
 NCLM: 424/186.100; 530/324.000  
 [7]  
 ICM: A61K039-145  
 EXF 435/5; 435/240.2; 424/184.1-189.1; 424/204.1-211.1; 424/225.1;  
 424/227.1; 424/230.1; 514/1; 514/2; 530/324; 530/350; 530/826  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 L12 ANSWER 5 OF 11 USPTAFULL  
 AN 2002:259381 USPTAFULL  
 TI Materials and methods relating to lipid metabolism  
 IN Ballinger, Dennis G., Menlo Park, CA, UNITED STATES  
 Loeb, Deborah, San Jose, CA, UNITED STATES  
 Montgomery, Julie R., Santa Cruz, CA, UNITED STATES  
 Tang, Y. Tom, San Jose, CA, UNITED STATES  
 Zhou, Ping, Cupertino, CA, UNITED STATES  
 Goodrich, Ryle, San Jose, CA, UNITED STATES  
 Liu, Chenghua, San Jose, CA, UNITED STATES  
 Asundi, Vinod, Foster City, CA, UNITED STATES  
 Zhao, Qing A., San Jose, CA, UNITED STATES  
 Wehrman, Tom, Stanford, CA, UNITED STATES  
 Drmanac, Radoje T., Palo Alto, CA, UNITED STATES  
 Ren, Feiyun, Cupertino, CA, UNITED STATES  
 Qian, Xiaohong B., San Jose, CA, UNITED STATES  
 Wang, Dunru, Poway, CA, UNITED STATES  
 PI US 2002142953 AI 20021003  
 AI US 2001-835956 AI 20010416 (9)  
 RLI Continuation-in-part of Ser. No. US 2000-714936, filed on 17 Nov 2000,  
 PENDING Continuation-in-part of Ser. No. US 2000-667298, filed on 22 Sep  
 2000, PENDING Continuation-in-part of Ser. No. US 2000-631451, filed on  
 3 Aug 2000, PENDING Continuation-in-part of Ser. No. US 2000-598042,  
 filed on 20 Jun 2000, PENDING  
 PRAI US 2000-197137P 20000414 (60)  
 FS Utility  
 INCL INCLM: 514/012.000  
 INCLM: 435/069.100; 435/325.000; 435/320.100; 530/359.000; 435/196.000;  
 536/023.200  
 NCLM: 514/012.000  
 NCLM: 435/069.100; 435/325.000; 435/320.100; 530/359.000; 435/196.000;  
 536/023.200  
 [7]  
 ICM: A61K038-17  
 EXF ICS: C07H021-04; C12N009-16; C12P021-02; C12N005-06; C07K014-775  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 L12 ANSWER 6 OF 11 USPTAFULL  
 AN 2002:206116 USPTAFULL  
 TI Toxicant-induced differential gene expression  
 IN Reichardt-Olson, John F., Montclair, NJ, UNITED STATES  
 PI US 2002110808 AI 20020815

AI US 2000-489220 AI 20000121 (9)  
 DT Utility  
 FS APPLICATION  
 INCL INCLM: 435/006.000  
 INCLM: 435/091.200; 536/023.100  
 NCLM: 435/006.000  
 NCLM: 435/091.200; 536/023.100  
 [7]  
 ICM: C12Q001-68  
 EXF ICS: C07H021-02; C07H021-04; C12P019-34  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 L12 ANSWER 7 OF 11 USPTAFULL  
 AN 2002:164658 USPTAFULL  
 TI Immunotherapeutic methods for extracorporeal modulation of CD36 and its  
 ligands  
 IN Srivastava, Pramod K., Avon, CT, UNITED STATES  
 PI US 2002086276 AI 20020704  
 AI US 2000-750973 AI 20001228 (9)  
 DT Utility  
 FS APPLICATION  
 INCL INCLM: 435/002.000  
 INCLM: 424/140.100  
 NCLM: 435/002.000  
 NCLM: 424/140.100  
 [7]  
 ICM: A61K039-395  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 L12 ANSWER 8 OF 11 USPTAFULL  
 AN 2002:136555 USPTAFULL  
 TI Methods of modulating an immune response to antigen, and cells for use  
 in the method  
 IN Segal, Andrew H., Boston, MA, United States  
 PA Whitehead Institute for Biomedical Research, Cambridge, MA, United  
 States (U.S. corporation)  
 PI US 6403080 B1 20020611  
 AI US 1999-339523 AI 19990624 (9)  
 RLI Division of Ser. No. US 1997-826259, filed on 27 Mar 1997, now patented,  
 Pat. No. US 5951976  
 PRAI US 1996-14364P 19960328 (60)  
 FS Utility  
 INCL INCLM: 424/093.100  
 INCLM: 424/093.200; 424/093.210; 424/093.700; 424/093.710; 424/136.100;  
 435/325.000; 514/002.000; 514/012.000; 530/387.300  
 NCLM: 424/093.100  
 NCLM: 424/093.200; 424/093.210; 424/093.700; 424/093.710; 424/136.100;  
 435/325.000; 514/002.000; 514/012.000; 530/387.300  
 [7]  
 ICM: A01N063-00  
 EXF ICS: A61K039-395; A61K038-00; C12P021-08  
 424/93.21; 424/93.7; 424/93.1; 424/93.2; 424/93.71; 424/136.1; 435/325;  
 514/12; 514/21; 530/387.3  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 L12 ANSWER 9 OF 11 USPTAFULL  
 AN 2002:66639 USPTAFULL  
 TI Compositions comprising heat shock proteins  
 or alpha(2) macroglobulin, antigenic molecules and saponins, and methods  
 of use thereof  
 IN Armen, Garo H., Manhasset, NY, UNITED STATES



PI US 2002037290 A1 20020328  
 AI US 2001-909778 A1 20010720 (9)  
 PRAI US 2000-223133P 20000807 (60)  
 DT Utility  
 FS APPLICATION  
 LN CNT 4136  
 INCL INCLM: 424/178.100  
 INCLS: 514/012.000; 514/026.000  
 NCLM: 424/178.100  
 NCLS: 514/012.000; 514/026.000  
 IC (7)  
 ICM: A61K039-395  
 ICS: A61K038-17  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 10 OF 11 USPATFULT  
 AN 2001:67794 USPATFULT  
 TI Human respiratory syncytial virus peptides with antitumorogenic and  
 antiviral activities  
 IN Barney, Shawn O'Lin, Cary, NC, United States  
 Lambert, Dennis Michael, Cary, NC, United States  
 Peterway, Stephen Robert, Cary, NC, United States  
 Trimeris, Inc., Durham, NC, United States (U.S. corporation)  
 PA US 1995-485264 B1 20010508  
 PI US 6228983  
 AI US 1995-485264 19950607 (8)  
 RLI Division of Ser. No. US 1995-470896, filed on 6 Jun 1995  
 Continuation-in-part of Ser. No. US 1994-360107, filed on 20 Dec 1994  
 Continuation-in-part of Ser. No. US 1994-255208, filed on 7 Jun 1994  
 Continuation-in-part of Ser. No. US 1993-73028, filed on 7 Jun 1993, now  
 patented, Pat. No. US 5464933

DT Utility  
 FS Granted  
 LN CNT 32166  
 INCL INCLM: 530/300.000  
 INCLS: 530/324.000; 530/325.000; 530/326.000; 424/211.100; 424/186.100  
 NCLM: 530/300.000  
 NCLS: 424/186.100; 424/211.100; 530/324.000; 530/325.000; 530/326.000  
 IC (7)  
 ICM: A61K038-00  
 EXF 530/350; 530/324-329; 530/300; 424/211.1  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 11 OF 11 USPATFULT  
 AN 1999:141305 USPATFULT  
 TI Adjuvant for transcutaneous immunization  
 IN Glenn, Gregory M., Bethesda, MD, United States  
 Alving, Carl R., Bethesda, MD, United States  
 PA The United States of America as represented by the U.S. Army Medical  
 Research & Materiel Command, Washington, DC, United States (U.S.  
 government)  
 PI US 5980898 19991109  
 AI US 1997-896885 19970717 (8)  
 RLI Continuation-in-part of Ser. No. US 1996-749164, filed on 14 Nov 1996  
 DT Utility  
 FS Granted  
 LN CNT 1988  
 INCL INCLM: 424/184.100  
 INCLS: 424/449.000; 424/450.000; 424/236.000; 424/240.100; 424/241.100;  
 424/275.100; 530/363.000; 530/403.000  
 NCLM: 424/184.100  
 NCLS: 424/085.100; 424/240.100; 424/241.100; 424/275.100; 424/449.000;  
 424/450.000; 530/363.000; 530/403.000  
 IC (6)  
 ICM: A61K039-00  
 ICS: C07K014-005; C07K014-195

EXF 424/449; 424/450; 424/184.1; 424/236; 424/240.1; 424/241.1; 424/275.1;  
 530/363; 530/403  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d kwic 11

L12 ANSWER 11 OF 11 USPATFULT  
 SUMM "Large molecules normally do not get across the intact  
 mammalian skin. It is thus impossible to immunize epicutaneously with  
 simple peptide or protein solutions." They concluded, "The  
 dermally applied liposomal or mixed micellar immunogens are biologically  
 as inactive as simple protein."  
 DETD Antigen obtained through recombinant means or peptide  
 synthesis, as well as antigen of the invention obtained from natural  
 sources or extracts, may be purified by means of:  
 DETD . . . granulocyte-monocyte-colony stimulating factor (reviewed in  
 Nobria and Rubin, 1994), a muramyl dipeptide derivative (e.g.,  
 murabutide, threonyl-MDP or muramyl tripeptide), a heat  
 shock protein or a derivative, a derivative of  
 Leishmania major Lef1 (Skelley et al., 1995), cholera toxin or cholera  
 toxin B, a . . .  
 DETD Optionally, an activator of langerhans cells may be used as an adjuvant.  
 Examples of such activators include: inducers of heat  
 shock protein; contact sensitizers (e.g.,  
 trinitrochlorobenzene, dinitrofluorobenzene, nitrogen mustard,  
 pentadecylcatechol); toxins (e.g., Shiga toxin, Staph enterotoxin B);  
 lipopolysaccharides, lipid A, or derivatives . . .  
 DETD . . . immune response to cholera toxin (CT) in rabbits and to a  
 tetra-peptides (Asn-Ala-Asn-Pro) conjugated to BSA. The  
 authors found that the immune response to cholera toxin or to the  
 synthetic malaria protein . . .  
 DETD . . . the groups could be detected. ETA differs from CT and LT in  
 that ETA is a single 613 amino acid peptide with A and B  
 domains on the same peptide and binds to an entirely different  
 receptor, the .alpha.2-macroglobulin  
 receptor/low density lipoprotein receptor-related protein  
 (Kounnas et al., 1992). Despite the dissimilarities between ETA and CT  
 in size, structure, and binding . . .  
 DETD Bodanszky, M. (1993) Peptide Chemistry, Springer-Verlag, New  
 York.  
 DETD . . . L. F., et al. (1992b) Safety, immunogenicity, and efficacy of a  
 Plasmodium falciparum vaccine comprising a circumsporozoite protein  
 repeat region peptide conjugated to Pseudomonas aeruginosa  
 toxin A. Infect. Immun., 60:1834-1839.  
 DETD Pesti, A., et al. (1991) Lack of H-2 restriction of the Plasmodium  
 falciparum (NANP) sequence as multiple antigen peptide. Eur.  
 J. Immunol., 24:2273-2276.  
 DETD Porcador, A., et al. (1997) Intranasal immunization with CTL epitope  
 peptides from HIV-1 or ovalbumin and the mucosal adjuvant  
 cholera toxin induces peptide-specific CTLs and protection  
 against tumor development in vivo. J. Immunol., 158:834-841.  
 DETD Schwarzenberger, K., and Udey, M. C. (1996) Contact allergens and  
 epidermal proinflammatory cytokines modulate langerhans cell  
 E-cadherin expression in situ. J. Invest. Dermatol., 106:553-558.  
 DETD Tan, J. P. (1988) Synthetic peptide vaccine design: Synthesis  
 and properties of a high-density multiple antigenic peptide  
 system. Proc. Natl. Acad. Sci. U.S.A., 85:5409-5413.  
 DETD Vandenberg, A. A., et al. (1996) Treatment of multiple sclerosis with  
 T-cell receptor peptides: Results of a double-blind pilot  
 trial. Nature Medicine, 2:1109-1115.  
 DETD Wang, R., et al. (1995) Induction of protective polyclonal antibodies by  
 immunization with a Plasmodium yoelii circumsporozoite protein multiple  
 antigen peptide vaccine. J. Immunol., 154:2784-2793.

- DETD Wisdom, G. B. (1994) **Peptide Antigens**, IRL Press, Oxford.
- => d kwic 9
- L12 ANSWER 9 OF 11 USPATFULL  
TI Compositions comprising heat shock proteins  
or alpha(2) macroglobulin, antigenic molecules and saponins, and methods  
of use thereof  
AB . . . diseases, and primary and metastatic neoplastic diseases. In  
the practice of the invention, the compositions are employed comprising:  
(a) a heat shock protein (hsp) or an  
alpha(2) macroglobulin (.alpha.2M); (b) a saponin; and, optionally, (c)  
an antigenic molecule. The antigenic molecule displays the antigenicity.
- SUMM . . . diseases (i.e., cancer), neurodegenerative or amyloid diseases,  
and autoimmune diseases, and methods of formulating the compositions.  
The compositions comprise a heat shock  
protein (hsp) or alpha(2) macroglobulin (.alpha.2M) and a saponin  
when used for the treatment and prevention of an autoimmune disease. The  
compositions.  
SUNM . . . Biology of the Cell, p. 1228). Both cytotoxic T cells and  
helper T cells recognize antigen in the form of peptide  
fragments that are generated by the degradation of foreign protein  
antigens inside the target cell, and both, therefore, depend on major  
histocompatibility complex (MHC) molecules, which bind these  
peptide fragments, carry them to the cell surface, and present  
them there to the T cells (Alberts et al., 1d.). MHC.  
SUNM . . . homology between them, and showed that gp96 and p84/86 were,  
respectively, the endoplasmic reticular and cytosolic counterparts of  
the same heat shock proteins (Srivastava  
et al., 1988, Immunogenetics 28:205-207; Srivastava et al., 1991, Curr.  
Top. Microbiol. Immunol. 167:109-123). Further, hsp70 was shown to .  
elicit immunity to the tumor from which it was isolated but not to  
antigenically distinct tumors. However, hsp70 depleted of  
peptides was found to lose its immunogenic activity (Udono and  
Srivastava, 1993, J. Exp. Med. 178:1351-1356). These observations  
suggested that the heat shock proteins are  
not immunogenic per se, but instead form noncovalent complexes with  
antigenic peptides, and the complexes elicit specific immunity  
to the antigenic peptides (Srivastava, 1993, Adv. Cancer Res.  
62:153-177; Udono et al., 1994, J. Immunol., 152:5398-5403; Suto et al.,  
1995, Science, 269:1585-1588).
- SUNM [0012] Noncovalent complexes of hsps and peptide, purified  
from cancer cells, can be used for the treatment and prevention of  
cancer and have been described in PCT. . . 17, 1998, respectively.  
each of which is incorporated by reference herein in its entirety). The  
isolation and purification of stress protein-peptide complexes  
has been described, for example, from pathogen-infected cells, and can  
be used for the treatment and prevention of infection.  
intracellular pathogens, including bacteria, protozoa, fungi and  
parasites (see e.g., PCT Publication WO 95/24923, dated Sep. 21, 1995).  
Immunogenic stress protein-peptide complexes can also be  
prepared by in vitro complexing of stress protein and antigenic  
peptides, and the uses of such complexes for the treatment and  
prevention of cancer and infectious diseases has been described in .  
publication WO 97/10000, dated Mar. 20, 1997 and U.S. Pat. No.  
6,030,618 issued Feb. 29, 2000. The use of stress protein-  
peptide complexes for sensitizing antigen presenting cells in  
vitro for use in adoptive immunotherapy is described in PCT publication  
WO 97/10002.
- SUNM [0013] 2.3. Heat Shock Proteins and Their  
Roles in Antigen Presentation  
SUNM [0014] 2.3.1. Heat Shock Proteins  
SUNM [0015] Heat shock proteins (hsps), also
- SUNM referred to as stress proteins, were first identified as proteins  
synthesized by cells in response to heat shock.  
[0016] Heat shock proteins are among the  
most highly conserved proteins in existence. For example, Dnak, the  
hsp70 from E. coli, has about 50% . . .  
SUNM . . . proteins in normal cells (Lindquist et al., 1988, Ann. Rev.  
Genetics 22:631-677). The hsps are capable of binding proteins or  
peptides, and of releasing the bound proteins or  
peptides in the presence of adenosine triphosphate (ATP) or low  
pH.  
SUNM . . . present antigens on the cell surface of antigen-presenting  
cells. Cytotoxic T lymphocytes (CTLs) then recognize MHC molecules and  
their associated peptides and kill the target cell. Antigens  
are processed by two distinct antigen processing routes depending upon  
whether their origin is . . .  
SUNM [0020] The heat shock protein gp96  
chaperones a wide array of peptides, depending upon the source  
from which gp96 is isolated (for review, see Srivastava et al., 1998,  
Immunology 8: 657-665). Tumor-derived gp96 carries tumor-antigenic  
peptides (Ishii et al., 1999, J. Immunology 162:1103-1109), gp96  
preparations from virus-infected cells carry viral epitopes (Suto and  
Srivastava, 1995, Science. . . (Arnold et al., 1995, J. Exp.  
Med. 182:885-889; Breloer et al., 1998, Eur. J. Immunol. 28:1016-1021).  
The association of gp96 with peptides occurs in vivo (Memozet  
and Srivastava, 1999, Biochem. Biophys. Research Commun. 262:813-818).  
gp96-peptide complexes, whether isolated from cells (Tamura et  
al., 1997, J. . . 186:1183-1406) are excellent immunogens and have  
been used extensively to elicit CD8+ T cell responses specific for the  
gp96-chaperoned antigenic peptides.  
SUNM [0021] The capacity of gp96-peptide complexes to elicit an  
immune response is dependent upon the transfer of the peptide  
to MHC class I molecules of antigen-presenting cells (Suto and  
Srivastava, 1995, supra). Endogenously synthesized antigens chaperoned  
by gp96 in CD8+ T cells (or MHC I-restricted CTLs) in vivo; this  
priming of CD8+ T cells requires macrophages. However, the process  
whereby exogenously-introduced gp96-peptide complexes elicit  
the antigen-specific CD8+ T cell response is not completely understood  
since there is no established pathway for the translocation of  
extracellular antigens into the class I presentation machinery. Yet  
antigenic peptides of extracellular origin associated with  
hsps are somehow salvaged by macrophages, channeled into the endogenous  
pathway, and presented by MHC.  
SUNM [0022] Several models have been proposed to explain the delivery of  
extracellular peptides for antigen presentation. One proposal,  
known as the "direct transfer" model, suggests that hsp-chaperoned  
peptides are transferred to MHC I molecules on the cell surface  
of macrophages for presentation to CD8+ T lymphocytes. Another  
suggestion. . . al., 1994, Immunogenetics 39:93-98). Others have  
suggested that a novel intracellular trafficking pathway may be involved  
for the transport of peptides from the extracellular medium  
into the lumen of the ER (Day et al., 1997, Proc. Natl. Acad. Sci.  
94:8064-8069; Nicchitta. . . the cytosol where it would enter the  
normal class I pathway; and/or (b) digest ingested material in lysosomes  
and reexport peptides for loading on the surface to class I  
molecules (Bevan, 1995, J. Exp. Med. 182:639-41).  
SUNM [0023] Still others have proposed a receptor-mediated pathway for the  
delivery of extracellular peptides to the cell surface of APCs  
for antigen presentation. In view of the extremely small quantity of  
gp96-chaperoned antigenic peptides required for immunization  
(Blachere et al., 1997, supra), and the strict dependence of  
immunogenicity of gp96-peptide complexes on functional APCs  
presenting cells (APCs) (Udono et al., 1994, Proc. Natl. Acad. Sci.  
U.S.A. 91:3077-3081), APCs had been . . . receptor is thought to be  
used in the uptake of gp96 (Clupitru et al., 1990, J. Exp. Med.,

187:685-691). The alpha(2)macroglobulin receptor, also known as CD91, has proven to be a more universal receptor for hsp90, with binding to gp96, hsp90, hsp70, . . . surfaces of other cells, the APCs. APCs can trap lymph- and blood-borne antigens and, after internalization and degradation, present antigenic peptide fragments, bound to cell-surface molecules of the major histocompatibility complex (MHC), to T cells. APCs may then activate T cells.

SUMM [0030] Alpha(2)macroglobulin promiscuously binds to proteins and peptides with nucleophilic amino acid side chains in a covalent manner (Chu et al., 1994, *Ann. N.Y. Acad. Sci.* 737:291-307) and . . . filed Jun. 2, 2000, which is incorporated by reference herein in its entirety). alpha.2M directly competes for the binding of heat shock protein gp96 to the alpha.2M, indicating that alpha.2M and hsp90 may bind to a common recognition site on the alpha.2M (Binder et al., 2000, *Nature Immunology* 1(2), 151-154). Additionally, alpha.2M-antigenic peptide complexes prepared in vitro can be administered to animals to generate a cytotoxic T cell response specific to the antigenic. . . Immunol. 166:4968-72). Thus, because hsp90 and alpha.2M have a number of common functional attributes, such as the ability to bind peptide, the recognition and uptake by the alpha.2M, and the stimulation of a cytotoxic T cell response, alpha.2M can be used.

SUMM (White et al., 1991, "A purified saponin acts as an adjuvant for a T-independent antigen," in: *Immunobiology of Proteins and Peptides*, Vol. VI (Kraus ed.), Plenum Press, New York, pp. 207-210). The immunogenicity of the vaccine was further increased by conjugating.

SUMM [0044] The ability of adjuvants to modulate the isotype distribution and IgG subclass distribution of antibody response to an antigen through the promotion of Ig subclass switching. . . substantially lack antigenic molecules, are particularly useful in treating an autoimmune disorder. "Antigenic molecule" as used herein refers to a peptide or other molecule with which hsp90 are endogenously associated in vivo (e.g., in precancerous or cancerous tissue), as well as . . . hsp90 are not complexed in vivo) or antigenic/immunogenic fragments and derivatives thereof. Such exogenous peptides and fragments and derivatives (both peptide and non-peptide) thereof for use in complexing with hsp90 or alpha.2M, can be selected from among those known in the art, as . . . cancer cell, a cell infected with an infectious organism or a cell or structure, e.g., extracellular deposits or plaques comprising peptide and/or protein fibrils, that displays the hallmarks of a neurodegenerative or amyloid disease. In certain embodiments, the outcome of eliciting . . . the saponin, and the antigenic molecule are combined simultaneously. In another embodiment, purified hsp90 or alpha.2M is stripped of bound peptide and antigenic molecule, or antigenic molecule previously covalently linked to saponin, is bound to said hsp90 or alpha.2M in vitro.

SUMM [0067] In accordance with the methods described herein, immunogenic or antigenic peptides that are endogenously complexed to hsp90 or alpha.2M can be used as specific antigenic molecules. For example, such peptides may be prepared that stimulate cytotoxic T cell responses against different tumor antigens (e.g., tyrosinase, gp100, melan-A, gp75, mucins, etc.), or a fragment thereof, or a prion protein, and their antigenic derivatives. In the embodiment wherein the antigenic molecules are peptides noncovalently complexed to hsp90 or alpha.2M in vivo, the complexes can be isolated from cells, or alternatively, produced in vitro.

SUMM . . . use specific antigenic molecules by complexing to hsp90 in vitro, hsp90 can be purified for such use from the endogenous hsp-peptide complexes in the presence of ATP or low pH (or chemically synthesized or recombinantly produced). The protocols described herein may be used to isolate hsp-peptide complexes.

SUMM or the hsp90 alone, from any eukaryotic cells for example, tissues, isolated cells, or immortalized eukaryotic cell lines infected. . . using recombinant methods known in the art (see Suzne et al., 1997, *Proc. Natl. Acad. Sci. U.S.A.* 94: 1146-51). alpha.2M-antigenic peptide fusions are then expressed and isolated. By specifically designing the antigenic peptide portion of the molecule, such fusion proteins can be used to elicit an immune response and in immunotherapy against target.

SUMM . . . of the above embodiments, is a synthetic or recombinantly generated peptide.

SUMM . . . cell, can be used in the present methods for producing alpha.2M polypeptide-antigenic molecule complexes. The cancer cells provide the antigenic peptides which become associated covalently or noncovalently with the expressed alpha.2M polypeptide. alpha.2M polypeptide-antigenic molecule complexes are then purified from the.

SUMM . . . vitro. Immunogenic alpha.2M polypeptide-antigenic molecule complexes can be generated in vitro by coupling of an alpha.2M polypeptide with an antigenic peptide. Procedures for forming such alpha.2M-antigenic molecule complexes and methods for isolating antigenic peptides are described below.

SUMM . . . the nucleophilic activation, employing heat (Gr-o flashed, n and Pizzo, 1998, *Biochemistry*, 37: 6009-6014). Such conditions that allow fortuitous trapping of peptides by alpha.2M are employed to prepare the alpha.2M-antigenic complexes for use in the invention. Methods for such covalent coupling.

SUMM . . . 2 hrs at 25 degree C. The preparations can be centrifuged through a Centricon 10 assembly (Millipore) to remove any unbound peptide. Alternatively, free antigenic molecule may be removed by passage over a gel permeation column. The association of the peptides with the alpha.2M polypeptide can be assayed by SDS-PAGE. This is the preferred method for in vitro complexing of antigenic molecules isolated from MHC-antigenic molecule complexes, or peptides dissociated from endogenous alpha.2M-antigenic molecule complexes.

SUMM [0111] 4.2.2. Preparation and Purification of hsp70-peptide Complexes

SUMM [0112] The purification of hsp70-peptide complexes has been described previously, see, for example, Udono et al., 1993, *J. Exp. Med.* 178:1391-1396. A procedure that may . . . [0115] Fractions strongly immunoreactive with the anti-hsp70 antibody are pooled and the hsp70-peptide complexes precipitated with ammonium sulfate; specifically with a 50%-70% ammonium sulfate cut. The resulting precipitate is then harvested by centrifugation.

SUMM [0116] The hsp70-peptide complex can be purified to apparent homogeneity using this method. Typically 1 mg of hsp70-peptide complex can be purified from 1 g of cells/tissue.

SUMM [0117] An improved method for purification of hsp70-peptide complexes comprises contacting cellular proteins with ADP or a nonhydrolyzable analog of ATP affixed to a solid substrate, such that. . . ADP affixed to a solid substrate (e.g., ADP-agarose). The resulting hsp70 preparations are higher in purity and devoid of contaminating peptides. The hsp70 yields are also increased significantly by about more than 10 fold. Alternatively, chromatography with nonhydrolyzable analogs of ATP, instead of ADP, can be used for purification of hsp70-peptide complexes. By way of example but not limitation, purification of hsp70-peptide complexes by ADP-agarose chromatography can be carried out as follows:

SUMM . . . ADP-agarose column. The column is washed in buffer and is eluted with 5 column volumes of 3 mM ADP. The hsp70-peptide complexes elute in fractions 2 through 10 of the total 15 fractions which elute. The eluted fractions are analyzed by SDS-PAGE. The hsp70-peptide complexes can be purified to apparent homogeneity using this procedure.

SUMM [0119] 4.2.3. Preparation and Purification of hsp90-peptide  
Complexes  
SUMM [0123] The eluted fractions are fractionated by SDS-PAGE and fractions  
containing the hsp90-peptide complexes identified by Western  
immunoblotting using an anti-hsp90 antibody such as 3G3 (Affinity  
Bioreagents). hsp90-peptide complexes can be purified to  
apparent homogeneity using this procedure. Typically, 150-200  $\mu$ g of  
hsp90-peptide complex can be purified from 1 g of  
cells/tissue.  
SUMM [0124] 4.2.4. Preparation and Purification of gp96-peptide  
Complexes  
SUMM . . . nuclei and other debris. The supernatant from this  
centrifugation step is then recentrifuged at 100,000 g for 90 minutes.  
The gp96-peptide complex can be purified either from the  
100,000 pellet or from the supernatant.  
SUMM . . . procedure, however, may be modified by two additional steps,  
used either alone or in combination, to consistently produce apparently  
homogeneous gp96-peptide complexes. One optional step involves  
an ammonium sulfate precipitation prior to the Con A purification step  
and the other optional . . .  
SUMM . . . concentrations of 2 mM, respectively. Then the sample is  
purified by either the unmodified or the modified method for isolating  
gp96-peptide complex from the 100,000 g supernatant, see  
above.  
SUMM [0134] The gp96-peptide complexes can be purified to apparent  
homogeneity using this procedure. About 10-20  $\mu$ g of gp96 can be  
isolated from 1 . . .  
SUMM [0135] 4.2.5. Preparation and Purification of hsp110-peptide  
Complexes  
SUMM [0139] 4.2.6. Preparation and Purification of grp170-peptide  
Complexes  
SUMM [0149] 4.2.10. Peptides from  $\alpha$ -2m or hsp-peptide  
Complexes  
SUMM [0150] Antigenic molecules (e.g. peptides) can be eluted from  
hsp-antigenic molecule complexes either in the presence of ATP or low  
pH. Antigenic molecules can be eluted from  $\alpha$ -2m-antigenic molecule  
complexes in the presence of low pH. These experimental conditions may  
be used to isolate peptides or non-peptide antigenic  
components from cells which may contain potentially useful antigenic  
determinants. Once isolated, the amino acid sequence of an antigenic  
peptide may be determined using conventional amino acid  
sequencing methodologies. Antigenic molecules can then be produced by  
chemical synthesis or recombinant . . .  
SUMM [0151] Thus, potentially immunogenic or antigenic peptides may  
be isolated from either endogenous stress protein-peptide  
complexes or endogenous MHC-peptide complexes for use  
subsequently as antigenic molecules, by complexing in vitro to hsp.  
SUMM . . . While the low molecular weight may be analyzed by HPLC as  
described below. In the ATP incubation protocol, the stress protein-  
peptide complex in the large molecular weight fraction is  
incubated with 10 mM ATP for 30 minutes at room temperature. In the low  
pH protocol, acetic acid or trifluoroacetic acid (TFA) is added to the  
stress protein-peptide complex to give a final concentration  
of 10% (vol/vol) and the mixture incubated at room temperature or in a  
boiling . . .  
SUMM . . . 10 assembly as mentioned previously. The high and low molecular  
weight fractions are recovered. The remaining large molecular weight  
stress protein-peptide complexes can be reincubated with ATP  
or low pH to remove any remaining peptides.  
SUMM . . . by developing the column with a linear gradient of 0 to 80%  
acetonitrile in 0.1% TFA. The elution of the peptides can be  
monitored by OD, sub. 210 and the fractions containing the  
peptides collected.  
SUMM [0155] 4.2.11. Peptides from MHC-peptide Complexes  
SUMM [0156] The isolation of potentially immunogenic peptides from

MHC molecules is well known in the art and so is not described in detail  
herein (See, Falk et al. . . .  
SUMM [0157] Briefly, MHC-peptide complexes may be isolated by a  
conventional immunofluorescence procedure. The peptides then may  
be eluted from the MHC-peptide complex by incubating the  
complexes in the presence of about 0.1% TFA in acetonitrile. The eluted  
peptides may be fractionated and purified by reverse phase HPLC,  
as before.  
SUMM [0158] The amino acid sequences of the eluted peptides may be  
determined either by manual or automated amino acid sequencing  
techniques well known in the art. Once the amino acid sequence of a  
potentially protective peptide has been determined the  
peptide may be synthesized in any desired amount using  
conventional peptide synthesis or other protocols well known  
in the art.  
SUMM [0159] Peptides having the same amino acid sequence as those  
isolated above may be synthesized by solid-phase peptide  
synthesis using procedures similar to those described by Merrifield,  
1963, J. Am. Chem. Soc. 85:2149. During synthesis, N $\alpha$ -alpha-protected  
amino acids . . . stepwise to a growing polypeptide chain linked by  
its C-terminal and to an insoluble polymeric support i.e., polystyrene  
beads. The peptides are synthesized by linking an amino group  
of an N $\alpha$ -alpha-protected amino acid to an  $\alpha$ -carboxy group of an  
N $\alpha$ -alpha-protected amino . . . it with a reagent such as  
dicyclohexylcarbodiimide. The attachment of a free amino group to the  
activated carboxyl leads to peptide bond formation. The most  
commonly used N $\alpha$ -alpha-protecting groups include Boc which is acid  
labile and Fmoc which is base labile.  
SUMM . . . is coupled to the activated  $\alpha$ -carboxylate group of the  
next N $\alpha$ -alpha-protected amino acid. The process is repeated until the  
desired peptide is synthesized. The resulting peptides  
are then cleaved from the insoluble polymer support and the amino acid  
side chains deprotected. Longer peptides can be derived by  
condensation of protected peptide fragments. Details of  
appropriate chemistries, resins, protecting groups, protected amino  
acids and reagents are well known in the art and so are not discussed in  
detail herein (See, Atherton et al., 1989, Solid Phase Peptide  
Synthesis: A Practical Approach, IRL Press, and Bodanszky, 1993,  
Peptide Chemistry, A Practical Textbook, 2nd Ed.,  
Springer-Verlag).  
SUMM [0161] Purification of the resulting peptides is accomplished  
using conventional procedures, such as preparative HPLC using gel  
permeation, partition and/or ion exchange chromatography. The choice of . . .  
SUMM . . . molecules associated with neurodegenerative diseases, or  
epitopes of antigenic molecules associated with amyloid diseases,  
including but not limited to fibril peptides or proteins, are  
used. For example, such neurodegenerative disease-associated antigenic  
molecules may be molecules associated with Alzheimer's Disease,  
age-related loss . . . proteins. Amyloid disease associated antigenic  
molecules may be molecules associated with diseases characterized by the  
extracellular deposition of protein and/or peptide fibrils  
which form amyloid deposits or plaques, including but not limited to  
type II diabetes and amyloidosis associated with chronic . . .  
SUMM [0173] In an embodiment in which complexes of hsp and the  
peptides with which they are endogenously associated in vivo are  
not employed, complexes of hsp to antigenic molecules are produced in  
vitro. As will be appreciated by those skilled in the art, the  
peptides either isolated by the aforementioned procedures or  
chemically synthesized or recombinantly produced may be reconstituted  
with a variety of purified . . .  
SUMM [0174] Prior to complexing, the hsp are pretreated with ATP or low pH  
to remove any peptides that may be associated with the hsp of  
interest. When the ATP procedure is used, excess ATP is removed from

SUMM . . . mm phenyl methyl sulfonyl fluoride (PMSF). The preparations are centrifuged through a Centricon 10 assembly (Millipore) to remove any unbound peptide. The association of the peptides with the stress proteins can be assayed by SDS-PAGE. This is the preferred method for in vitro complexing of peptides isolated from MHC-peptide complexes of peptides disassociated from endogenous hsp-peptide complexes.

SUMM [0177] In an alternative embodiment of the invention, preferred for producing complexes of gp96 or hsp90 to peptides, 5-10 micrograms of purified gp96 or hsp90 is incubated with equimolar or excess quantities of the antigenic peptide in a suitable buffer such as one containing 20 mM sodium phosphate buffer pH 7.5, 0.5M NaCl, 3 mM MgCl<sub>2</sub>. . . room temperature and centrifuged one or more times if necessary, through a Centricon 10 assembly (Millipore) to remove any unbound peptide.

SUMM [0182] Additional embodiments of the invention relate to pharmaceutical compositions comprising either .alpha.2M or an hsp, optionally a peptide (which need not be antigenic), and a saponin adjuvant, for the prevention or treatment of an autoimmune disorder. These compositions.

SUMM . . . the carboxyl group on the glucuronic acid of saponins from Quilaja saponaria Molina can be conjugated to a protein, a peptide, or a small molecule containing a primary amine. According to Higuchi et al., 1987, Phytochemistry 26:229, saponins from Quilaja saponaria.

SUMM . . . human patient) is applied at 20 degree C. for 1 hour, and the plates are washed 3 times with PBS-T. The anti-peptide antibody activity is then measured calorimetrically after incubating at 20 degree C. for 1 hour with 50 .mu.l/well of sheep anti-mouse.

SUMM . . . of this method, peripheral blood mononuclear cells from a subject treated with a given tumor or with peptide antigen(s) of an agent of infectious disease. Cells are then stained with T cell-specific labeled antibodies detectable by flow cytometry.

SUMM . . . 274: 94-96) may be used to identify antigen-specific T-cells. For example, in one embodiment, an MHC molecule containing a specific peptide antigen, such as a tumor-specific antigen, is multimerized to make soluble peptide tetramers and labeled, for example, by complexing to streptavidin. The MHC-peptide antigen complex is then mixed with a population of T cells obtained from a subject treated with a composition of .

SUMM . . . be used to modify individual nucleotides in a DNA sequence, for purpose of making amino acid substitution(s) in the expressed peptide sequence, or for creating/deleting restriction sites to facilitate further manipulations. Such techniques include but are not limited to, chemical mutagenesis.

SUMM . . . incorporated herein by reference, demonstrates that deletion of the ER retention signal of gp96 results in the secretion of gp96-Ig peptide-complexes from transfected tumor cells, and that fusion of the KDEL-deleted gp96 with murine IgG1 facilitated its detection by ELISA and.

SUMM . . . be used to modify individual nucleotides in a DNA sequence, for purpose of making amino acid substitution(s) in the expressed peptide sequence, or for creating/deleting restriction sites to facilitate further manipulations. Such techniques include but are not limited to, chemical mutagenesis.

SUMM . . . done prior to administration, before or after the compositions of the invention are formulated, wherein covalent complexing of an endogenous hsp-peptide complex is desired, the complex is preferably cross-linked after purification from cells or tissues. In one embodiment, antigenic molecules are . . . in a preferred embodiment, glutaraldehyde crosslinking may be used. Glutaraldehyde crosslinking has been used for formation of covalent complexes of peptides and hsp (see Barrios et al., 1992, Eur. J. Immunol. 22: 1365-1372). Preferably, 1-2 mg of complex is crosslinked in . . . at (see, for example, Shankarappa et al., 1992, PCR Method Appl. 1:277-278). The

SUMM DNA fragment that encodes .alpha.2M, or the peptide-binding domain thereof, is then isolated, and ligated into an appropriate expression vector, care being taken to ensure that the proper . . . purification from the cells in which they are expressed. For example, an .alpha.2M polypeptide may contain a signal sequence leader peptide to direct its translocation across the ER membrane for secretion into culture medium. Further, an .alpha.2M polypeptide may contain an . . . affinity label, such as an affinity label, fused to any portion of the .alpha.2M polypeptide not involved in binding antigenic peptide, such as for example, the carboxyl terminal. The affinity label can be used to facilitate purification of the protein, by . . .

SUMM . . . frame into a vector containing the sequence of an affinity label, such that the .alpha.2M polypeptide is expressed as a peptide-tagged fusion protein. Affinity labels, which may be recognized by specific binding partners, may be used for affinity purification of the . . .

SUMM . . . .alpha.2M polypeptide novel structural properties, such as the ability to form multimers. Dimerization of an .alpha.2M polypeptide with a bound peptide may increase avidity of interaction between the .alpha.2M polypeptide and its partner in the course of antigen presentation. These affinity. . .

SUMM . . . involved in disulfide bonding with other cysteines in the Ig molecule. Since none of the cysteines are required for the peptide to function as a tag, one or more of these cysteine residues may optionally be substituted by another amino acid. . . for the efficient secretion of .alpha.2M polypeptide from bacterial and mammalian cells (von Heijne, 1985, J. Mol. Biol. 184:99-105). Leader peptides are selected based on the intended host cell, and may include bacterial, yeast, viral, animal, and mammalian sequences. For example, the herpes virus glycoprotein D leader peptide is suitable for use in a variety of mammalian cells. A preferred leader peptide for use in mammalian cells can be obtained from the V-12-C region of the mouse immunoglobulin kappa chain (Bernard et . . .

SUMM [0261] DNA sequences encoding a desired affinity label or leader peptide, which may be readily obtained from libraries, produced synthetically, or may be available from commercial suppliers, are suitable for the . . .

SUMM [0272] For long-term, high-yield production of properly processed hsp-peptide complexes, stable expression in mammalian cells is preferred. Cell lines that stably express hsp or .alpha.2M and antigenic molecules to produce hsp-peptide complexes for incorporating into the compositions of the present invention may be engineered by using a vector that contains a . . . repeat (LTR), a 3' LTR, a packaging signal, a bacterial origin of replication, and a selectable marker. The ND-associated antigenic peptide DNA is inserted into a position between the 5' LTR and 3' LTR, such that transcription from the 5' LTR . . .

SUMM . . . of the present invention include but are not limited to are diseases characterized by the extracellular deposition of protein and/or peptide fibrils which form amyloid deposits or plaques, including but not limited to type II diabetes and amyloidoses associated with chronic. . .

SUMM . . . done prior to administration, before or after the compositions of the invention are formulated, wherein covalent complexing of an endogenous hsp-peptide complex is desired, the complex is preferably cross-linked after purification from cells or tissues. In one embodiment, antigenic molecules are . . . in a preferred embodiment, glutaraldehyde crosslinking may be used. Glutaraldehyde crosslinking has been used for formation of covalent complexes of peptides and hsp (see Barrios et al., 1992, Eur. J. Immunol. 22: 1365-1372). Preferably, 1-2 mg of complex is crosslinked in . . . adoptive immunotherapy using APC sensitized with hsp- or .alpha.2M-antigenic molecule complexes. As described in Section 4.10

herein, the hsp- or .alpha.2M-peptide complex-sensitized APC can be administered alone, in combination claimed compositions, or before or after administration of the claimed compositions. Furthermore, . . .

15 minutes to 24 hours. By way of example but not limitation, 4.times.10.sup.7 macrophages can be incubated with 10 microgram gp96-peptide complexes per ml or 100 microgram hsp90-peptide complexes per ml at 37.degree. C. for 15 minutes-24 hours in 1 ml plain RPMI medium. The cells are washed. . .

of a putative biomarker for risk of a specific cancer are measured to monitor the effect of hsp bound to peptide complexes. For example, in individuals at enhanced risk for prostate cancer, serum prostate-specific antigen molecule (PSA) is measured by the . . .

will be understood that, where reference is made to an antigenic molecule as a component of a composition, an antigenic peptide or full-length protein may be used (e.g. having more than 50 amino acid residues). The amount of an antigenic molecule. . .

day interval, either (i) phosphate buffer saline (PBS), (ii) 0.1, 1, 10, 25, 50, or 100 .mu.g/mouse of, for example, gp96-peptide complexes derived from UV6138 carcinomas, or (iii) 0.1, 1, 10, 25, 50, or 100 .mu.g/mouse of gp96-peptide complexes derived from UV31698J carcinoma. For each dosage of gp96-peptide complex, 0, 1.6, 10, 20, 50, or 100 .mu.g of saponin fraction QS-21 (reconstituted in PBS from lyophilized powder) is mixed with the gp96-peptide complexes and coadministered. Control sets of mice receive the dosage series of QS-21 alone. . .

(10391) Coadministration of one or more saponins along with gp96-peptide complexes will elicit the desired immune response using reduced levels of the gp96-peptide complexes as compared to gp96-peptide complexes administered alone (i.e. in the absence of saponin). Accordingly, the invention provides the advantage of permitting reduction of the amount of an hsp or .alpha.2M-peptide complex required to elicit a desired immune response for prevention or treatment of cancer or infectious disease. . .

a second group receive, every other day for a total of five injections, 6, 1, 0.6, or 0.1 .mu.g/mouse of gp96-peptide complex derived from UV61398J carcinoma cells. Mice in a third group receive, in a similar manner, a total of five injections of gp96-peptide complex derived from normal liver. Mice in a fourth group receive, in a similar manner, a total of five injections of gp96-peptide complex derived from the UV61398J carcinoma cells, mixed with 20 or 100 .mu.g of QS-21. The mice in the fifth group receive, in a similar manner, a total of five injections of gp96-peptide complex derived from normal liver mixed with 20 or 100 .mu.g QS-21. Finally, the mice in the sixth group receive. . .

the liver-derived gp96 or in untreated mice (see U.S. Pat. No. 5,837,251). These results indicated a therapeutic effect of gp96 peptide complexes in the UV61398J carcinoma model. All mice eventually succumbed to tumor growth. A scrutiny of the kinetics of tumor growth in treated and control mice shows that administration of tumor-derived gp96-peptide complex had an immediate inhibitory effect on tumor growth and that the effect appears to diminish after treatment with gp96-peptide complex is terminated. . .

(10403) Coadministration of QS-21 with gp96-peptide complex derived from UV61398J carcinoma cells will result in a retardation of tumor growth when using smaller amounts of gp96-peptide complex as compared to the group receiving gp96-peptide complex from UV61398J carcinoma cells without QS-21. The administration of QS-21 alone, or gp96-peptide complex from normal liver plus QS-21, will not result in any significant difference as compared to the PBS control, or gp96-peptide complex from normal liver, respectively. . .

growth of established tumors using reduced amounts of the hsp

or .alpha.2M when saponin adjuvant is present. Additionally, recombinantly-expressed antigenic peptide -.alpha.2M or -hsp fusion proteins can also be employed to elicit immunosuppression of new tumors and retarded growth of established. . .

What is claimed is:  
1. A pharmaceutical composition comprising a purified heat shock protein (hsp) and a saponin.

=> d his

(FILE 'HOME' ENTERED AT 15:25:49 ON 20 FEB 2003)

FILE 'MEDLINE, CANCERLIT, BIOSIS, CONFSCI, EMBASE, CAPLUS, USPATFULL'  
ENTERED AT 15:26:27 ON 20 FEB 2003  
72563 S HEAT (A) SHOCK (A) PROTEIN  
40 S L1 AND ALPHA (A) 2 (A) MACROGLOBULIN (A) RECEPTOR  
L1  
L2 33 DUP REM L2 (7 DUPLICATES REMOVED)  
L3 12721 S L1 AND ANTIBOD?  
L4 21 S L4 AND L2  
L5 19 DUP REM L5 (2 DUPLICATES REMOVED)  
L6 1585 S ACONISTY AND L1  
L7 4 S L7 AND L2  
L8 8637 S L1 AND PEPTIDE?  
L9 27 S L9 AND L2  
L10 24 DUP REM L10 (3 DUPLICATES REMOVED)  
L11 11 S L11 AND MODULATE?  
L12

=> s alpha (a) 2 (a) macroglobulin (a) receptor  
L13 1624 ALPHA (A) 2 (A) MACROGLOBULIN (A) RECEPTOR  
L14

=> s l13 and modulat?  
L14 160 L13 AND MODULAT?

=> dup rem l14  
PROCESSING COMPLETED FOR L14  
L15 110 DUP REM L14 (50 DUPLICATES REMOVED)

=> s l15 and heat (a) shock (a) protein  
6 FILES SEARCHED...  
L16 14 L15 AND HEAT (A) SHOCK (A) PROTEIN

=> d 1-14

L16 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2003 ACS  
AN 2002:937303 CAPLUS  
DN 138:20443  
TI Endocrine disruptor screening using DNA chips of endocrine  
disruptor-responsive genes  
IN Kondo, Akhiro, Takeda, Takeshi; Mizutani, Shigetoshi; Tsujimoto,  
Yoshimasa; Takashima, Ryokichi; Enoki, Yuki; Kato, Ikunobu  
PA Takara Bio Inc., Japan  
SO Jpn. Kokai Tokkyo Koho, 386 pp.  
CODEN: JKKXAF

DT Patent  
LA Japanese  
FAN: CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002355079	A2	20021210		
JP 2001-73183	A	20010314	JP 2002-69354	20020313
JP 2001-74993	A	20010315		
JP 2001-102519	A	20010330		

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001/07373	A2	20011018	WO 2001-DE1486	20010406
W:	AE, AG, AL, AM, AT, AU, A2,	BA, BB, BG, BR, BY, BZ, CA, CH, CN,			
	CR, CU, CZ, DK, DM, DZ, EE, ES,	FI, GB, GD, GE, GH, GM, HR, HU,			
	ID, IL, IN, IS, JP, KE, KG, KP,	KK, KZ, LK, LR, LS, LT, LU,			
	LV, MA, MD, MG, MK, MN, MW, MX,	MK, NZ, NL, N2, PL, PT, RO, RU, SD,			
	SE, SG, SI, SK, SL, TJ, TM, TR,	TU, TZ, UA, UG, US, UZ, VN, YU,			
	ZA, ZW, AM, AZ, BY, BG, KZ, MD,	RJ, TM			
RM:	GH, GM, KE, LS, MM, MZ, SD, SL,	SZ, T2, ZC, ZW, AT, BE, CH, CY,			
	DE, DK, ES, FI, FR, GB, GR, IE,	IT, IT, LU, MC, NL, PT, SE, TR, BF,			
JF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
DE 10019058	A1	20011220		DE 2000-10019058	20000406
WO 2001/07373	A2	20011018		NO 2000-1X1486	20010406
W:	AE, AG, AL, AM, AT, AU, A2,	BA, BB, BG, BR, BY, BZ, CA, CH, CN,			
	CR, CU, CZ, DK, DM, DZ, EE, ES,	FI, GB, GD, GE, GH, GM, HR, HU,			
	ID, IL, IN, IS, JP, KE, KG, KP,	KZ, LC, LK, LR, LS, LT, LU,			
	LV, MA, MD, MG, MK, MN, MW, MX,	MK, NZ, NL, N2, PL, PT, RO, RU, SD,			
	SE, SG, SI, SK, SL, TJ, TM, TR,	TU, TZ, UA, UG, UZ, VN, YU, ZA,			
	ZW, AM, AZ, BY, BG, KZ, MD, RU,	TJ, TM			
RM:	GH, GM, KE, LS, MM, MZ, SD, SL,	SZ, T2, ZC, ZW, AT, BE, CH, CY,			
	DE, DK, ES, FI, FR, GB, GR, IE,	IT, IT, LU, MC, NL, PT, SE, TR, BF,			
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
WO 2001/07373	A2	20011018		EP 2001-XB1486	20010406
W:	AE, AG, AL, AM, AT, AU, A2,	BA, BB, BG, BR, BY, BZ, CA, CH, CN,			
	CR, CU, CZ, DK, DM, DZ, EE, ES,	FI, GB, GD, GE, GH, GM, HR, HU,			
	ID, IL, IN, IS, JP, KE, KG, KP,	KZ, LC, LK, LR, LS, LT, LU,			
	LV, MA, MD, MG, MK, MN, MW, MX,	MK, NZ, NL, N2, PL, PT, RO, RU, SD,			
	SE, SG, SI, SK, SL, TJ, TM, TR,	TU, TZ, UA, UG, UZ, VN, YU, ZA,			
	ZW, AM, AZ, BY, BG, KZ, MD, RU,	TJ, TM			
RM:	GH, GM, KE, LS, MM, MZ, SD, SL,	SZ, T2, ZC, ZW, AT, BE, CH, CY,			
	DE, DK, ES, FI, FR, GB, GR, IE,	IT, IT, LU, MC, NL, PT, SE, TR, BF,			
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
EP 1274865	A2	20030115		EP 2001-953936 -	20010406
R:	AT, BE, CH, DE, DK, ES, FI, FR,	GB, GR, GT, IT, LI, LU, NL, SE, MC, PT,			
	IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
EP 1278892	A1	20030129		EP 2001-940158	20010406
R:	AT, BE, CH, DE, DK, ES, FI, FR,	GB, GR, GT, IT, LI, LU, NL, SE, MC, PT,			
	IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRAI	DE 2000-10019058	A	20000406		
	DE 2000-10019173	A	20000630		
	DE 2000-10032523	A	20000630		
	DE 2000-10043826	A	20000901		
	WO 2001-DE1486	W	20010406		
	WO 2001-EP3969	W	20010406		
L16	ANSWER 5 OF 14	USPATFUL			
AN	2003:40533	USPATFUL			
IN	Methods for the inhibition of Epstein-Barr virus transmission employing anti-viral peptides capable of abrogating viral fusion and transmembrane				
	Barney, Shawn O'lin, Cary, NC, United States				
	Lambeck, Dennis Michael, Cary, NC, United States				
	Pettersen, Stephen Robert, Cary, NC, United States				
PA	Timeeris, Inc., Durham, NC, United States (U.S. corporation)				
AI	US 6518013	B1	20030201		
PI	US 1995-485546		19950607 (8)		
RLI	Continuation-in-part of Ser. No. US 1994-360107, filed on 20 Dec 1994, now patented, Pat. No. US 615036 Continuation-in-part of Ser. No. US 1994-255208, filed on 7 Jun 1994 Continuation-in-part of Ser. No. US 1993-75028, filed on 7 Jun 1993, now patented, Pat. No. US 5464933				
DT	Utility				
FS	GRANTED				
LN	CNT 24700				
INCL	INCMS: 434/005.000				
	INCMS: 426/330.100; 530/300.000; 530/324.000; 530/325.000; 530/326.000				

NCL NCLM: 435/005.000  
NCLS: 424/230.100; 530/300.000; 530/324.000; 530/325.000; 530/326.000

IC [7]  
ICM: C120001-70

EXF 435/5; 530/300; 530/324-329; 530/350; 424/230.1  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L16 ANSWER 6 OF 14 USPATFULT  
AN 2002:315069 USPATFULT  
TI Compositions and methods for treatment of neoplastic disease  
PI Terman, David S., Pebble Beach, CA, UNITED STATES  
IN US 2002177551 A1 20021128  
AI US 2001-870759 A1 20010530 (9)  
PRAI US 2000-208128P 20000531 (60)  
DT Utility  
FS APPLICATION

LN CNT 17323  
INCL INCLM: 514/012.000  
NCLS: 435/325.000; 530/350.000  
NCLM: 514/012.000  
NCLS: 435/325.000; 530/350.000

IC [7]  
ICM: A61K038-17  
ICS: C12N005-06; C07K014-705  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L16 ANSWER 7 OF 14 USPATFULT  
AN 2002:297296 USPATFULT  
TI Methods for inhibition of membrane fusion-associated events, including respiratory syncytial virus transmission  
IN Bolognesi, Dani Paul, Durham, NC, United States  
Matthews, Thomas James, Durham, NC, United States  
Wild, Carl T., Durham, NC, United States  
Barney, Shawn O'lin, Cary, NC, United States  
Lambert, Dennis Michael, Cary, NC, United States  
Petterway, Stephen Robert, Cary, NC, United States  
Langlois, Alphonse J., Durham, NC, United States  
Triemeris, Inc., Durham, NC, United States (U.S. corporation)  
PI US 6478055 B1 20021112  
AI US 1993-470896 19950606 (8)  
Continuation-in-part of Ser. No. US 1994-360107, filed on 20 Dec 1994, now patented, Pat. No. US 6017536 Continuation-in-part of Ser. No. US 1994-255208, filed on 7 Jun 1994 Continuation-in-part of Ser. No. US 1993-73028, filed on 7 Jun 1993, now patented, Pat. No. US 5464933

DT Utility  
FS GRANTED

LN CNT 26553  
INCL INCLM: 424/211.100  
NCLS: 424/186.100; 530/324.000  
NCLM: 424/211.100  
NCLS: 424/186.100; 530/324.000

IC [7]  
ICM: A61K039-145  
EXF 435/5; 435/240.2; 424/184.1-189.1; 424/204.1-211.1; 424/225.1; 424/227.1; 424/230.1; 514/1; 514/2; 530/324; 530/350; 530/826  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L16 ANSWER 8 OF 14 USPATFULT  
AN 2002:259381 USPATFULT  
TI Materials and methods relating to lipid metabolism  
IN Ballinger, Dennis G., Menlo Park, CA, UNITED STATES  
Loeb, Deborah, San Jose, CA, UNITED STATES  
Montgomery, Julie R., Santa Cruz, CA, UNITED STATES  
Tang, Y. Tom, San Jose, CA, UNITED STATES  
Zhou, Ping, Cupertino, CA, UNITED STATES

Goodrich, Ryle, San Jose, CA, UNITED STATES  
Liu, Chenghua, San Jose, CA, UNITED STATES  
Asundi, Vinod, Foster City, CA, UNITED STATES  
Zhao, Qing A., San Jose, CA, UNITED STATES  
Wehrman, Tom, Stanford, CA, UNITED STATES  
Derman, Radoje T., Palo Alto, CA, UNITED STATES  
Ren, Feiyang, Cupertino, CA, UNITED STATES  
Qian, Xiaohong B., San Jose, CA, UNITED STATES  
Wang, Duntui, Poway, CA, UNITED STATES  
AI US 2001-835996 A1 20010416 (9)  
US 2002142953 A1 20021003  
Continuation-in-part of Ser. No. US 2000-714936, filed on 17 Nov 2000, PENDING Continuation-in-part of Ser. No. US 2000-667298, filed on 22 Sep 2000, PENDING Continuation-in-part of Ser. No. US 2000-631451, filed on 3 Aug 2000, PENDING Continuation-in-part of Ser. No. US 2000-598042, filed on 20 Jun 2000, PENDING

PRAI US 2000-197137P 20000414 (60)  
DT Utility  
FS APPLICATION

LN CNT 9120  
INCL INCLM: 514/012.000  
NCLS: 435/069.100; 435/325.000; 435/320.100; 530/359.000; 435/196.000; 536/023.200  
NCLM: 514/012.000  
NCLS: 435/069.100; 435/325.000; 435/320.100; 530/359.000; 435/196.000; 536/023.200

IC [7]  
ICM: A61K038-17  
ICS: C07H021-04; C12N009-16; C12P021-02; C12N005-06; C07K014-775  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L16 ANSWER 9 OF 14 USPATFULT  
AN 2002:206116 USPATFULT  
TI Toxicant-induced differential gene expression  
IN Reidhaar-Olson, John F., Montclair, NJ, UNITED STATES  
PI US 2002110808 A1 20020815  
AI US 2000-489220 A1 20000121 (9)  
DT Utility  
FS APPLICATION

LN CNT 5161  
INCL INCLM: 435/006.000  
NCLS: 435/091.200; 536/023.100  
NCLM: 435/006.000  
NCLS: 435/091.200; 536/023.100

IC [7]  
ICM: C12Q001-68  
ICS: C07H021-02; C07H021-04; C12P019-34  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L16 ANSWER 10 OF 14 USPATFULT  
AN 2002:164658 USPATFULT  
TI Immunotherapeutic methods for extracorporeal modulation of CD36 and its ligands  
IN Srivastava, Pramod K., Avon, CT, UNITED STATES  
PI US 2002086376 A1 20020704  
AI US 2000-758973 A1 20001228 (9)  
DT Utility  
FS APPLICATION

LN CNT 1813  
INCL INCLM: 435/002.000  
NCLS: 424/140.100  
NCLM: 435/002.000  
NCLS: 424/140.100

IC [7]  
ICM: A61K039-395



CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L16 ANSWER 11 OF 14 USPATFUL  
AN 2002:136555 USPATFUL  
TI Methods of modulating an immune response to antigen, and cells  
for use in the method  
IN Segal, Andrew H., Boston, MA, United States  
PA Whitehead Institute for Biomedical Research, Cambridge, MA, United  
States (U.S. corporation)  
PI US 6403080 B1 20020611  
AI US 1999-339523 19990624 (9)  
RLI Division of Ser. No. US 1997-826259, filed on 27 Mar 1997, now patented,  
Pat. No. US 5951976  
PRAI US 1996-14364P 19960328 (60)  
PS Utility  
DS GRANTED  
LN.CNT 2153  
INCL INCLM: 424/093.100  
INCLS: 424/093.200; 424/093.210; 424/093.700; 424/093.710; 424/136.100;  
424/136.100; 424/093.100  
NCLM: 424/093.100  
NCLS: 424/093.200; 424/093.210; 424/093.700; 424/093.710; 424/136.100;  
424/136.100; 514/002.000; 514/012.000; 530/387.300  
IC [7]  
ICM: A01N063-00  
EXF ICS: A61K039-395; A61K038-00; C12P021-08  
424/93.21; 424/93.7; 424/93.1; 424/93.2; 424/93.71; 424/136.1; 424/136.100;  
514/12; 514/21; 530/387.3  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
L16 ANSWER 12 OF 14 USPATFUL  
AN 2002:66639 USPATFUL  
TI Compositions comprising heat shock proteins  
or alpha(2) macroglobulin, antigenic molecules and saponins, and methods  
of use thereof  
IN Armen, Gary H., Mahanaset, NY, UNITED STATES  
PI US 2002037290 A1 20020328  
AI US 2001-309778 A1 20010720 (9)  
PRAI US 2000-223133P 20000807 (60)  
DS Utility  
FS APPLICATION  
LN.CNT 4136  
INCL INCLM: 424/178.100  
INCLS: 514/012.000; 514/026.000  
NCLM: 424/178.100  
NCLS: 514/012.000; 514/026.000  
IC [7]  
ICM: A61K039-395  
ICS: A61K038-17  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
L16 ANSWER 13 OF 14 USPATFUL  
AN 2001:67794 USPATFUL  
TI Human respiratory syncytial virus peptides with antitumor and  
antiviral activities  
IN Barney, Shawn O'lin, Cary, NC, United States  
Lambert, Dennis Michael, Cary, NC, United States  
Petterway, Stephen Robert, Cary, NC, United States  
Tilmeris, Inc., Durham, NC, United States (U.S. corporation)  
PI US 6228993 B1 20010508  
AI US 1995-485264 19950607 (8)  
RLI Division of Ser. No. US 1995-470896, filed on 6 Jun 1995  
Continuation-in-part of Ser. No. US 1994-360107, filed on 20 Dec 1994  
Continuation-in-part of Ser. No. US 1994-255208, filed on 7 Jun 1994  
Continuation-in-part of Ser. No. US 1993-73028, filed on 7 Jun 1993, now

patented, Pat. No. US 5464933

DT Utility  
PS Granted  
LN.CNT 32166  
INCL INCLM: 530/300.000  
INCLS: 530/324.000; 530/325.000; 530/326.000; 424/211.100; 424/186.100  
NCLM: 530/300.000  
NCLS: 424/186.100; 424/211.100; 530/324.000; 530/325.000; 530/326.000  
IC [7]  
ICM: A61K038-00  
EXF 530/350; 530/324-329; 530/300; 424/211.1  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
L16 ANSWER 14 OF 14 USPATFUL  
AN 1999:141305 USPATFUL  
TI Adjuvant for transcutaneous immunization  
IN Glenn, Gregory M., Bethesda, MD, United States  
PA Alving, Carl R., Bethesda, MD, United States  
The United States of America as represented by the U.S. Army Medical  
Research & Materiel Command, Washington, DC, United States (U.S.  
government)  
PI US 5980898 19991109  
AI US 1997-896085 19970717 (8)  
RLI Continuation-in-part of Ser. No. US 1996-749164, filed on 14 Nov 1996  
DS Utility  
FS Granted  
LN.CNT 1988  
INCL INCLM: 424/184.100  
INCLS: 424/449.000; 424/450.000; 424/236.000; 424/240.100; 424/241.100;  
424/275.100; 530/363.000; 530/403.000  
NCLM: 424/184.100  
NCLS: 424/085.100; 424/240.100; 424/241.100; 424/275.100; 424/449.000;  
424/450.000; 530/363.000; 530/403.000  
IC [6]  
ICM: A61K039-00  
ICS: C07K014-005; C07K014-195  
EXF 424/449; 424/450; 424/184.1; 424/236; 424/240.1; 424/241.1; 424/275.1;  
530/363; 530/403  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
=> d his  
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FILE 'MEDLINE, CANCERLIT, BIOSIS, CONFSCI, EMBASE, CAPLUS, USPATFUL.'  
ENTERED AT 15:26:27 ON 20 FEB 2003  
L1 72563 S HEAT (A) SHOCK (A) PROTEIN  
L2 40 S L1 AND ALPHA (A) 2 (A) MACROGLOBULIN (A) RECEPTOR  
L3 33 DUP REM L2 (7 DUPLICATES REMOVED)  
L4 12721 S L1 AND ANTIBODY?  
L5 21 S L4 AND L2  
L6 19 DUP REM L5 (2 DUPLICATES REMOVED)  
L7 1585 S ACONIST? AND L1  
L8 4 S L7 AND L2  
L9 8637 S L1 AND PEPTIDE?  
L10 27 S L9 AND L2  
L11 24 DUP REM L10 (3 DUPLICATES REMOVED)  
L12 11 S L11 AND MODULATE?  
L13 1624 S ALPHA (A) 2 (A) MACROGLOBULIN (A) RECEPTOR  
L14 160 S L13 AND MODULATE?  
L15 110 DUP REM L14 (50 DUPLICATES REMOVED)  
L16 14 S L15 AND HEAT (A) SHOCK (A) PROTEIN  
=> s l14 and peptid?

L17 50 L14 AND PEPTID?

=> dup rem 117  
PROCESSING COMPLETED FOR L17  
L18 50 DUP REM L17 (0 DUPLICATES REMOVED)

=> d 1-50

L18 ANSWER 1 OF 50 USPATFULL  
AN 2003:37603 USPATFULL  
TI Human CDNA's and proteins and uses thereof  
IN Benjamin, Stephane, Paris, FRANCE  
PA GENSET, S.A., Paris, FRANCE, 75008 (non-U.S. corporation)  
PI US 2003027248 AI 20030206  
AI US 2001-924340 AI 20010806 (9)  
PRAI US 2001-305456P 20010713 (60)  
US 2001-302277P 20010629 (60)  
US 2001-298698P 20010615 (60)  
US 2001-293574P 20010525 (60)  
DT Utility  
FS APPLICATION  
LN.CNT 25650  
INCL INCLM: 435/069.100; 435/320.100; 435/325.000; 530/350.000; 536/023.200;  
NCLM: 435/066.000  
NCLM: 435/069.100; 435/320.100; 435/325.000; 530/350.000; 536/023.200;  
IC [7]  
ICM: C12P021-02  
ICS: C12001-68; C07H021-04; C12N009-00; C12N005-06

L18 ANSWER 2 OF 50 USPATFULL  
AN 2003:37516 USPATFULL  
TI Human CDNA's and proteins and uses thereof  
IN Benjamin, Stephane, Paris, FRANCE  
PA GENSET, S.A., Paris, FRANCE, 75008 (non-U.S. corporation)  
PI US 2003027161 AI 20030206  
AI US 2001-992600 AI 20011113 (9)  
R1 Division of Ser. No. US 2001-924340, filed on 6 Aug 2001, PENDING  
PRAI WO 2001-181715 20010806  
US 2001-305456P 20010713 (60)  
US 2001-302277P 20010629 (60)  
US 2001-298698P 20010615 (60)  
US 2001-293574P 20010525 (60)  
DT Utility  
FS APPLICATION  
LN.CNT 25529  
INCL INCLM: 435/066.000  
INCLM: 435/069.100; 435/183.000; 435/320.100; 435/325.000; 530/350.000;  
NCLM: 435/066.000  
NCLM: 435/069.100; 435/183.000; 435/320.100; 435/325.000; 530/350.000;  
IC [7]  
ICM: C12001-68  
ICS: A01K067-00; C07H021-04; C12N009-00; C12P021-02; C12N005-06

L18 ANSWER 3 OF 50 USPATFULL  
AN 2003:37187 USPATFULL  
TI Anticlonal liposomes for delivery of bioactive agents  
IN Lakkaraju, Aparna, Minneapolis, MN, UNITED STATES  
Dubinsky, Janet M., St. Paul, MN, UNITED STATES

L18 ANSWER 4 OF 50 USPATFULL  
AN 2003:30238 USPATFULL  
TI Secreted protein HMP03  
IN Fischer, Carrie L., Burke, VA, UNITED STATES  
Rosen, Craig A., Laytonville, MD, UNITED STATES  
Soppet, Daniel R., Centreville, VA, UNITED STATES  
Ruben, Steven M., Olney, MD, UNITED STATES  
Kyaw, Hla, Frederick, MD, UNITED STATES  
Li, Yi, Sunnyvale, CA, UNITED STATES  
Zeng, Zhishen, Lansdale, PA, UNITED STATES  
Lafleur, David W., Washington, DC, UNITED STATES  
Moore, Paul A., Germantown, MD, UNITED STATES  
Sui, Yangu, Galtersburg, MD, UNITED STATES  
Olsen, Henrik S., Galtersburg, MD, UNITED STATES  
Ebner, Reinhard, Galtersburg, MD, UNITED STATES  
Brewer, Laurie A., St. Paul, MN, UNITED STATES  
US 2003022185 AI 20030130  
US 2001-983802 AI 20011025 (9)  
Continuation of Ser. No. US 1999-227357, filed on 8 Jan 1999, GRANTED,  
Pat. No. US 6342581 Continuation-in-part of Ser. No. WO 1998-0513684,  
filed on 7 Jul 1998, UNKNOWN  
PRAI US 1997-51928P 19970708 (60)  
US 1997-52793P 19970708 (60)  
US 1997-51928P 19970708 (60)  
US 1997-51928P 19970708 (60)  
US 1997-52803P 19970708 (60)  
US 1997-52732P 19970708 (60)  
US 1997-51931P 19970708 (60)  
US 1997-51932P 19970708 (60)  
US 1997-51916P 19970708 (60)  
US 1997-51930P 19970708 (60)  
US 1997-51918P 19970708 (60)  
US 1997-51928P 19970708 (60)  
US 1997-52735P 19970708 (60)  
US 1997-52795P 19970708 (60)  
US 1997-51919P 19970708 (60)  
US 1997-51928P 19970708 (60)  
US 1997-55722P 19970818 (60)  
US 1997-55723P 19970818 (60)  
US 1997-55948P 19970818 (60)  
US 1997-55949P 19970818 (60)  
US 1997-55953P 19970818 (60)  
US 1997-55950P 19970818 (60)  
US 1997-55947P 19970818 (60)  
US 1997-55964P 19970818 (60)  
US 1997-56360P 19970818 (60)  
US 1997-55684P 19970818 (60)  
US 1997-55984P 19970818 (60)  
US 1997-55954P 19970818 (60)  
US 1997-58785P 19970912 (60)  
US 1997-58664P 19970912 (60)  
US 1997-58660P 19970912 (60)

L18 ANSWER 5 OF 50 USPATFULL  
AN 2003:30238 USPATFULL  
TI Secreted protein HMP03  
IN Fischer, Carrie L., Burke, VA, UNITED STATES  
Rosen, Craig A., Laytonville, MD, UNITED STATES  
Soppet, Daniel R., Centreville, VA, UNITED STATES  
Ruben, Steven M., Olney, MD, UNITED STATES  
Kyaw, Hla, Frederick, MD, UNITED STATES  
Li, Yi, Sunnyvale, CA, UNITED STATES  
Zeng, Zhishen, Lansdale, PA, UNITED STATES  
Lafleur, David W., Washington, DC, UNITED STATES  
Moore, Paul A., Germantown, MD, UNITED STATES  
Sui, Yangu, Galtersburg, MD, UNITED STATES  
Olsen, Henrik S., Galtersburg, MD, UNITED STATES  
Ebner, Reinhard, Galtersburg, MD, UNITED STATES  
Brewer, Laurie A., St. Paul, MN, UNITED STATES  
US 2003022185 AI 20030130  
US 2001-983802 AI 20011025 (9)  
Continuation of Ser. No. US 1999-227357, filed on 8 Jan 1999, GRANTED,  
Pat. No. US 6342581 Continuation-in-part of Ser. No. WO 1998-0513684,  
filed on 7 Jul 1998, UNKNOWN  
PRAI US 1997-51928P 19970708 (60)  
US 1997-52793P 19970708 (60)  
US 1997-51928P 19970708 (60)  
US 1997-51928P 19970708 (60)  
US 1997-52803P 19970708 (60)  
US 1997-52732P 19970708 (60)  
US 1997-51931P 19970708 (60)  
US 1997-51932P 19970708 (60)  
US 1997-51916P 19970708 (60)  
US 1997-51930P 19970708 (60)  
US 1997-51918P 19970708 (60)  
US 1997-51928P 19970708 (60)  
US 1997-52735P 19970708 (60)  
US 1997-52795P 19970708 (60)  
US 1997-51919P 19970708 (60)  
US 1997-51928P 19970708 (60)  
US 1997-55722P 19970818 (60)  
US 1997-55723P 19970818 (60)  
US 1997-55948P 19970818 (60)  
US 1997-55949P 19970818 (60)  
US 1997-55953P 19970818 (60)  
US 1997-55950P 19970818 (60)  
US 1997-55947P 19970818 (60)  
US 1997-55964P 19970818 (60)  
US 1997-56360P 19970818 (60)  
US 1997-55684P 19970818 (60)  
US 1997-55984P 19970818 (60)  
US 1997-55954P 19970818 (60)  
US 1997-58785P 19970912 (60)  
US 1997-58664P 19970912 (60)  
US 1997-58660P 19970912 (60)

L18	ANSWER OF 50	CAPLUS	COPYRIGHT 2003	ACS	
DN	137381503				
TI	Compositions and methods for modulating Dlx-mediated protein interactions and their diagnostic and therapeutic uses				
IN	Allen, Kristina; Antkowiak, Anthony; Bhat, Bheem M.; Danaaghe, Veronique; Robinson, John Allen; Yavorsky, Paul J.				
PA	Genome Therapeutics Corporation, USA; Wyeth, John and Brother Ltd.				
SO	PCT Int. Appl., 376 pp.				
DT	Patent				
LA	English				
FAN	CNT 3				
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 2002092015	A2	20021121	WO 2002-US15982	20020517
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NO, NZ, OM, PA, PG, PH, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, BG, KZ, MD, RU, TJ, TM				
RN:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GN, GU, GW, ML, MR, NE, SN, TD, TG				
PRAI	US 2001-293131	P	20010517		
US	2002-353058	P	20020201		
US	2002-361293	P	20020304		
L18	ANSWER 8 OF 50	CAPLUS	COPYRIGHT 2003	ACS	
DN	1372736374				
TI	Protein-protein interactions of C/EBP and diagnosis and treatment of				
IN	Proinflammatory immune response and other diseases				
PA	Cimpora, Daniel M.; Heltman, Karen; Bartel, Paul L.				
SO	Myriad Genetics, Inc., USA				
DT	PCT Int. Appl., 47 pp.				
LA	English				
FAN	CNT 3				
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 2002074919	A2	20020926	WO 2002-US8025	20020315
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NO, NZ, OM, PA, PG, PH, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, BG, KZ, MD, RU, TJ, TM, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GN, GU, GW, ML, MR, NE, SN, TD, TG				
PRAI	US 2002197626	A1	20021226	US 2002-98192	20020315
PRAI	US 2001-276037	P	20010316		
L18	ANSWER 9 OF 50	CAPLUS	COPYRIGHT 2003	ACS	
DN	136145258				
TI	Methods for the treatment of neural disorders with agents that bind to				
IN	low-d. lipoprotein receptor-related protein receptors				
PA	Hyman, Bradley T.; Scitricland, Dudley K.; Baccala, Brian J.; Rebeck, G. William				
SO	The General Hospital Corporation, USA; The American National Red Cross				

SO PCT Int. Appl., 50 PP.  
 DT CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

PI WO 2002007755 A1 20020131 WO 2000-US40636 20000815

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NZ, NL, NO, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TW, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, BG, BR, CA, CH, CN, CU, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, BM, GM, KE, LS, MM, MZ, SD, SI, SZ, TZ, UG, ZW, AT, BE, CH, CY, CF, CG, CI, CM, GN, GW, ML, MR, NE, SN, TD, TG

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 10 OF 50 CAPLUS COPYRIGHT 2003 ACS  
 AN 2002:850252 CAPLUS  
 DN 137:363083  
 TI Methods of suppressing microglial activation by administering compounds binding to microglial receptors  
 IN Laikowitz, Daniel T.; Matthew, William D.; McMillian, Michael  
 PA USA  
 SO U.S. Pat. Appl. Publ., 25 pp., Cont.-in-part of U. S. Ser. No. 260,430.  
 DT Patent  
 LA English  
 FAN.CNT 2

PATENT NO. KIND DATE APPLICATION NO. DATE

PI US 2002164789 A1 20021107 US 2001-957909 20010921  
 PRAI US 1998-77551P P 19980311  
 US 1999-260430 A2 19990301

L18 ANSWER 11 OF 50 CAPLUS COPYRIGHT 2003 ACS  
 AN 2002:937303 CAPLUS  
 DN 138:20443  
 TI Endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes  
 IN Kondo, Akihito; Takeda, Takeshi; Mizutani, Shigetoshi; Tsujimoto, Yoshinaga; Takashima, Ryokichi; Enoki, Yuki; Kato, Ikunoshin  
 PA Takara Bio Inc., Japan  
 SO Jpn. Kokai Tokkyo Koho, 386 pp.  
 DT Patent  
 LA Japanese  
 FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

PI JP 2002355079 A2 20021210 JP 2002-69354 20020313  
 PRAI JP 2001-73183 A 20010315  
 JP 2001-74993 A 20010315  
 JP 2001-102519 A 20010330

L18 ANSWER 12 OF 50 USPATFUL  
 AN 2002:315069 USPATFUL  
 TI Compositions and methods for treatment of neoplastic disease  
 IN Terman, David S.; Pebble Beach, CA, UNITED STATES  
 PI US 2002177551 A1 20021128  
 US 2001-870759 A1 20010530 (9)

PRAI US 2000-208128P 20000531 (60)  
 DT Utility  
 FS APPLICATION  
 LN.CNT 17323

INCL INCLM: 514/012.000  
 NCLM: 435/325.000; 530/350.000  
 NCLM: 514/012.000  
 NCLM: 435/325.000; 530/350.000

IC [7]  
 ICM: A61K038-17  
 ICS: C07H021-04; C12N009-16; C12P021-02; C12N005-06; C07K014-775  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L18 ANSWER 13 OF 50 USPATFUL  
 AN 2002:2259381 USPATFUL  
 TI Materials and methods relating to lipid metabolism  
 IN Leob, Deborah; San Jose, CA, UNITED STATES  
 BAilinger, Dennis G.; Menlo Park, CA, UNITED STATES  
 Montgomey, Julie R.; Santa Cruz, CA, UNITED STATES  
 Tang, Y. Tom; San Jose, CA, UNITED STATES  
 Zhou, Ping; Cupertino, CA, UNITED STATES  
 Goodrich, Ryle; San Jose, CA, UNITED STATES  
 Liu, Chenghua; San Jose, CA, UNITED STATES  
 Asundi, Vinod; Foster City, CA, UNITED STATES  
 Zhao, Qing A.; San Jose, CA, UNITED STATES  
 Weinman, Tom; Stanford, CA, UNITED STATES  
 Drmanac, Radoje T.; Palo Alto, CA, UNITED STATES  
 Ren, Feiyan; Cupertino, CA, UNITED STATES  
 Qian, Xiaohong B.; San Jose, CA, UNITED STATES  
 Wang, Dunrui; Poway, CA, UNITED STATES  
 US 2001-835996 A1 20010416 (9)  
 US 2001-42953 A1 20021003  
 US 2001-835996 A1 20010416 (9)  
 Continuation-in-part of Ser. No. US 2000-714936, filed on 17 Nov 2000.  
 PENDING Continuation-in-part of Ser. No. US 2000-667298, filed on 22 Sep 2000.  
 PENDING Continuation-in-part of Ser. No. US 2000-631451, filed on 3 Aug 2000.  
 PENDING Continuation-in-part of Ser. No. US 2000-598042, filed on 20 Jun 2000.  
 20000414 (60)

PRAI US 2000-197137P 20000414 (60)  
 DT Utility  
 FS APPLICATION  
 LN.CNT 9120

INCL INCLM: 514/012.000  
 NCLM: 435/069.100; 435/325.000; 435/320.100; 530/359.000; 435/196.000;  
 NCLM: 514/012.000  
 NCLM: 435/069.100; 435/325.000; 435/320.100; 530/359.000; 435/196.000;  
 NCLM: 514/012.000

IC [7]  
 ICM: A61K038-17  
 ICS: C07H021-04; C12N009-16; C12P021-02; C12N005-06; C07K014-775  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L18 ANSWER 14 OF 50 USPATFUL  
 AN 2002:242764 USPATFUL  
 TI Compositions and methods for modulating muscle cell and tissue contractility  
 IN Cines, Douglas B.; Wymewood, PA, UNITED STATES  
 Higazi, Adal-Roof, Jerusalem, ISRAEL  
 PA The Trustees of the University of Pennsylvania (U.S. corporation)  
 PI US 2002131964 A1 20020919  
 US 2001-880503 A1 20010613 (9)  
 PRAI US 2000-212874P 20000620 (60)  
 DT Utility  
 FS APPLICATION  
 LN.CNT 3572

INCL INCLM: 424/094.630  
NCL NCLM: 424/094.630  
IC [7]  
ICM: A61K038-48  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L18 ANSWER 15 OF 50 USPATFULT  
AN 2002:206116 USPATFULT  
TI Toxicant-induced differential gene expression  
IN Reihart-Olson, John F., Montclair, NJ, UNITED STATES  
PI US 2002110808 AI 20020815  
AI US 2000-489220 AI 20000121 (9)  
DT Utility  
FS APPLICATION  
LN.CNT 5161  
INCL INCLM: 435/006.000  
NCL INCLM: 435/091.200; 536/023.100  
NCLM: 435/006.000  
NCLS: 435/091.200; 536/023.100  
IC [7]  
ICM: C120001-68  
ICS: C07H021-02; C07H021-04; C12P019-34  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L18 ANSWER 16 OF 50 USPATFULT  
AN 2002:164658 USPATFULT  
TI Immunotherapeutic methods for extracellular modulation of  
IN CD36 and its ligands  
IN Sriastava, Pramod K., Avon, CT, UNITED STATES  
PI US 2002068276 AI 20020704  
AI US 2000-750973 AI 20001228 (9)  
DT Utility  
FS APPLICATION  
LN.CNT 1813  
INCL INCLM: 435/002.000  
NCL INCLM: 424/140.100  
NCLM: 435/002.000  
NCLS: 424/140.100  
IC [7]  
ICM: A61K039-395  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L18 ANSWER 17 OF 50 USPATFULT  
AN 2002:105967 USPATFULT  
TI Complex for transferring an anionic substance of interest into a cell  
IN Rittner, Karola, Straasburg, FRANCE  
PI US 2002055174 AI 20020509  
AI US 2001-865553 AI 20010529 (9)  
PRAI EP 2000-440162 20000526  
EP 2001-440049 20010227  
US 2000-246083P 20001107 (60)  
US 2001-277982P 20010323 (60)  
DT Utility  
FS APPLICATION  
LN.CNT 1919  
INCL INCLM: 435/463.000  
NCL INCLM: 530/350.000  
NCLM: 435/463.000  
NCLS: 530/350.000  
IC [7]  
ICM: C12N015-87  
ICS: C07K014-00  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L18 ANSWER 18 OF 50 USPATFULT  
AN 2002:66639 USPATFULT  
TI Compositions comprising heat shock proteins or alpha(2) macroglobulin,  
IN antigenic molecules and saponins, and methods of use thereof  
PI Armen, Gato H., Manhasset, NY, UNITED STATES  
AI US 2002037290 AI 20020328  
PRAI US 2001-909778 AI 20010720 (9)  
US 2000-223133P 20000807 (60)  
DT Utility  
FS APPLICATION  
LN.CNT 4136  
INCL INCLM: 424/178.100  
NCL INCLM: 514/012.000; 514/026.000  
NCLM: 424/178.100  
NCLS: 514/012.000; 514/026.000  
IC [7]  
ICM: A61K039-395  
ICS: A61K038-17  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L18 ANSWER 19 OF 50 USPATFULT  
AN 2002:297236 USPATFULT  
TI Methods for inhibition of membrane fusion-associated events, including  
IN respiratory syncytial virus transmission  
Bolognesi, Dani Paul, Durham, NC, United States  
Matthews, Thomas James, Durham, NC, United States  
Wald, Carl T., Durham, NC, United States  
Barney, Shawn O'Lin, Cary, NC, United States  
Lambert, Dennis Michael, Cary, NC, United States  
Petteaway, Stephen Robert, Cary, NC, United States  
Langlois, Alphonse J., Durham, NC, United States  
Trimeris, Inc., Durham, NC, United States (U.S. corporation)  
PI US 6479055 BI 20021112  
AI US 1995-470896 19950606 (8)  
RI Continuation-in-part of Ser. No. US 1994-360107, filed on 20 Dec 1994,  
now patented, Pat. No. US 6017536 Continuation-in-part of Ser. No. US  
1994-255208, filed on 7 Jun 1994 Continuation-in-part of Ser. No. US  
1993-73028, filed on 7 Jun 1993, now patented, Pat. No. US 5464933  
DT Utility  
FS GRANTED  
LN.CNT 26553  
INCL INCLM: 424/211.100  
NCL INCLM: 424/186.100; 530/324.000  
NCLM: 424/211.100  
NCLS: 424/186.100; 530/324.000  
IC [7]  
ICM: A61K039-145  
EXF 435/5; 435/240.2; 424/184.1-189.1; 424/204.1-211.1; 424/225.1;  
424/227.1; 424/230.1; 514/1; 514/2; 530/324; 530/350; 530/826  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L18 ANSWER 20 OF 50 USPATFULT  
AN 2002:136555 USPATFULT  
TI Methods of modulating an immune response to antigen, and cells  
IN for use in the method  
Segal, Andrew H., Boston, MA, United States  
PA Whitehead Institute for Biomedical Research, Cambridge, MA, United  
States (U.S. corporation)  
PI US 6403080 BI 20020611  
AI US 1999-339523 19990624 (9)  
RLI Division of Ser. No. US 1997-826259, filed on 27 Mar 1997, now patented,  
Pat. No. US 5951976  
PRAI US 1996-14364P 19960328 (60)  
DT Utility  
FS GRANTED

LN CNT 2153  
INCL INCLM: 424/093.100  
INCLM: 424/093.200; 424/093.210; 424/093.700; 424/093.710; 424/136.100;  
NCLM: 435/325.000; 514/002.000; 514/012.000; 530/387.300  
NCLM: 424/093.100  
NCLM: 424/093.200; 424/093.210; 424/093.700; 424/093.710; 424/136.100;  
NCLM: 435/325.000; 514/002.000; 514/012.000; 530/387.300  
IC [7]  
ICM: A01N063-00  
ICS: A61K038-00; C12P021-08  
EXF 424/93.21; 424/93.7; 424/93.1; 424/93.2; 424/93.71; 424/136.1; 435/325;  
514/12; 514/21; 530/387.3  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L18 ANSWER 21 OF 50 USPTAFULL  
AN 2002.19393 USPTAFULL  
TI Secreted protein HLMFP03  
IN Rosen, Craig A., Laytonville, MD, United States  
Ruben, Steven M., Olney, MD, United States  
Olsen, Henrik S., Galtersburg, MD, United States  
Ebner, Reinhard, Galtersburg, MD, United States  
Human Genome Sciences, Inc., Rockville, MD, United States (U.S. Corporation)  
PI US 6342581 B1 20020129  
AI US 1999-227357 19990108 (9)  
R1I Continuation-in-part of Ser. No. WO 1998-US13684, filed on 7 Jul 1998  
PRAI US 1997-58785P 19970912 (60)  
US 1997-58664P 19970912 (60)  
US 1997-58660P 19970912 (60)  
US 1997-58661P 19970912 (60)  
US 1997-55722P 19970818 (60)  
US 1997-55723P 19970818 (60)  
US 1997-55948P 19970818 (60)  
US 1997-55949P 19970818 (60)  
US 1997-55953P 19970818 (60)  
US 1997-55950P 19970818 (60)  
US 1997-55947P 19970818 (60)  
US 1997-55964P 19970818 (60)  
US 1997-55660P 19970818 (60)  
US 1997-55664P 19970818 (60)  
US 1997-55984P 19970818 (60)  
US 1997-51926P 19970708 (60)  
US 1997-51925P 19970708 (60)  
US 1997-51925P 19970708 (60)  
US 1997-51928P 19970708 (60)  
US 1997-52803P 19970708 (60)  
US 1997-52732P 19970708 (60)  
US 1997-51931P 19970708 (60)  
US 1997-51932P 19970708 (60)  
US 1997-51916P 19970708 (60)  
US 1997-51930P 19970708 (60)  
US 1997-51918P 19970708 (60)  
US 1997-51920P 19970708 (60)  
US 1997-52733P 19970708 (60)  
US 1997-52795P 19970708 (60)  
US 1997-51918P 19970708 (60)  
US 1997-51928P 19970708 (60)  
DT Utility  
FS GRANTED  
LN CNT 18742  
INCL INCLM: 530/300.000  
INCLM: 530/350.000; 435/069.100  
NCLM: 530/300.000  
NCLM: 435/069.100; 530/350.000

IC [7]  
ICM: A61K038-00  
ICS: C07K001-00; C12P021-06  
EXF 530/300; 530/350; 435/69.1  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L18 ANSWER 22 OF 50 CAPLUS COPYRIGHT 2003 ACS  
AN 2002.840857 CAPLUS  
TI The cytoplasmic domain of the LDL receptor-related protein regulates multiple steps in APP processing  
AU Pierzick, Claus U.; Buesse, Tracy; Meriam, David E.; Weggen, Sascha; Koo, Edward H.  
CS Department of Neurosciences, University of California, San Diego, La Jolla, CA, 92093 USA  
SO EMBO Journal (2002), 21(21), 5691-5700  
CODEN: EMODJG; ISSN: 0261-4189  
PB Oxford University Press  
DT Journal  
LA English  
RE CNT 44  
THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 23 OF 50 CAPLUS COPYRIGHT 2003 ACS  
AN 2001.886449 CAPLUS  
DN 136.36328  
TI Alpha 2 macroglobulin receptors as a heat shock protein receptor and uses thereof  
IN Srivastava, Pramod K.  
PA University of Connecticut Health Center, USA  
SO PCT Int. Appl., 236 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN CNT 1  
PATENT NO. KIND DATE APPLICATION NO. DATE  
PI WO 2001092474 A1 20011206 WO 2001-US18041 20010604  
W: AU, CA, JP  
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR  
PRAI US 2000-20905P P 20000602  
US 2000-625137 A 20000725  
US 2000-668724 A 20000922  
US 2000-750972 A 20001228  
RE CNT 1  
THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 24 OF 50 CAPLUS COPYRIGHT 2003 ACS  
AN 2001.763235 CAPLUS  
DN 135.314399  
TI Detection of variations in the DNA methylation profile of genes in the determining the risk of disease  
IN Berlin, Kurt; Piepenbrock, Christian; Olek, Alexander  
PA Biogenomics A.-G., Germany  
SO PCT Int. Appl., 636 pp.  
CODEN: PIXXD2  
DT Patent  
LA German  
FAN CNT 68  
PATENT NO. KIND DATE APPLICATION NO. DATE  
PI WO 2001077373 A2 20011018 WO 2001-DE1486 20010406  
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,



RLI Continuation-in-part of Ser. No. US 1994-344836, filed on 23 Nov 1994,  
now abandoned Continuation-in-part of Ser. No. WO 1994-SE483, filed on  
24 May 1994  
PRAI SE 1993-1764 19930524  
DT Utility  
FS Granted  
LN CNT 1058  
INCL INCLM: 536/024.300  
INCLM: 514/044.000; 536/024.100  
NCLM: 536/024.300  
NCLM: 536/024.100  
IC [7]  
ICM: A61K031-7105  
ICS: A61K031-711; C07H021-04  
514/44; 536/24.1; 536/24.3  
EXF INDEXING IS AVAILABLE FOR THIS PATENT.  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
L18 ANSWER 29 OF 50 USPTATFULT  
AN 2001:79131 USPTATFULT  
TI Family of protease inhibitors, and other biologic active substances  
IN Voerman, Gerard, Brassaach, Belgium  
PA Clodica, S.A., Luxembourg, Luxembourg (non-U.S. corporation)  
PI US 6239106 B1 20010529  
PI WO 9613585 19960509  
AI US 1998-836686 \* 19980327 (8)  
WO 1995-EP4223 19951027  
19980327 PCT 371 date  
19980327 PCT 102(e) date  
PRAI EP 1994-117053 19941028  
EP 1995-103637 19950314  
DT Utility  
FS Granted  
LN CNT 813  
INCL INCLM: 514/013.000  
INCLM: 435/212.000; 435/213.000; 435/214.000; 435/215.000; 435/216.000;  
435/217.000; 435/218.000; 435/219.000; 435/069.100; 435/252.300;  
435/320.100; 536/023.200; 530/324.000; 530/350.000  
NCLM: 514/013.000  
NCLM: 435/069.100; 435/212.000; 435/213.000; 435/214.000; 435/215.000;  
435/216.000; 435/217.000; 435/218.000; 435/219.000; 435/252.300;  
435/320.100; 530/324.000; 530/350.000; 536/023.200  
IC [7]  
ICM: A61K038-00  
ICS: C12N009-48; C12N001-20; C07H021-04  
514/13; 435/212-219; 435/69.1; 435/252.3; 435/320.1; 536/23.2; 530/324;  
530/350  
EXF INDEXING IS AVAILABLE FOR THIS PATENT.  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
L18 ANSWER 30 OF 50 USPTATFULT  
AN 2001:67794 USPTATFULT  
TI Human respiratory syncytial virus peptides with anti-fusogenic  
and antiviral activities  
IN Barney, Shawn O'lin, Cary, NC, United States  
Lambert, Dennis Michael, Cary, NC, United States  
Patteway, Stephen Robert, Cary, NC, United States  
Triemstra, Inc., Durham, NC, United States (U.S. corporation)  
PI US 6238983 B1 20010508  
PI US 1995-485264 19950607 (8)  
Division of Ser. No. US 1995-470896, filed on 6 Jun 1995  
Continuation-in-part of Ser. No. US 1994-360107, filed on 20 Dec 1994  
Continuation-in-part of Ser. No. US 1994-255208, filed on 7 Jun 1994  
Continuation-in-part of Ser. No. US 1993-73028, filed on 7 Jun 1993, now  
patented, Pat. No. US 5464933  
DT Utility  
FS Granted

LN CNT 32166  
INCL INCLM: 530/300.000  
INCLM: 530/324.000; 530/325.000; 530/326.000; 424/211.100; 424/186.100  
NCLM: 530/300.000  
NCLM: 530/300.000  
IC [7]  
ICM: A61K038-00  
ICS: 530/350; 530/324-329; 530/300; 424/211.1  
EXF INDEXING IS AVAILABLE FOR THIS PATENT.  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
L18 ANSWER 31 OF 50 USPTATFULT  
AN 2001:63243 USPTATFULT  
TI Suppression of inhibitors  
IN Brunner, Nils, Hellerup, Denmark  
R.O. slashed.met, John, Copenhagen, Denmark  
Ellis, Vincent, Woodford Green, United Kingdom  
Pyke, Charles, Hiller.o slashed.d, Denmark  
Gr.o slashed.ndahl-Hansen, Jan, Holte, Denmark  
Pedersen, Helle, Aller.o slashed.d, Denmark  
Hansen, Heine H.o slashed.i, Holte, Denmark  
Dan.o slasheded., Keld, Charlottelund, Denmark  
PA Cancerforskningsfonden AF 1989, Copenhagen K, Denmark (non-U.S.  
corporation)  
PI US 6224865 B1 20010501  
PI US 1996-583129 19960515 (8)  
AI WO 9502413 19950126  
WO 1994-DK288 19940718  
19960515 PCT 371 date  
19960515 PCT 102(e) date  
PRAI DK 1993-851 19930716  
DT Utility  
FS Granted  
LN CNT 2471  
INCL INCLM: 424/130.100  
INCLM: 421/138.100; 421/141.100; 421/145.100; 421/155.100; 421/152.100;  
421/158.100; 421/172.100; 421/179.100; 421/181.100; 421/183.100;  
514/002.000  
NCLM: 424/130.100  
NCLM: 424/138.100; 424/141.100; 424/145.100; 424/152.100; 424/155.100;  
424/158.100; 424/172.100; 424/179.100; 424/181.100; 424/183.100;  
514/002.000  
IC [7]  
ICM: A61K039-395  
ICS: A01N037-18  
424/152.1; 424/141.1; 424/145.1; 424/155.1; 424/130.1; 424/138.1;  
424/158.1; 424/172.1; 424/179.1; 424/181.1; 424/183.1; 514/2  
EXF INDEXING IS AVAILABLE FOR THIS PATENT.  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
L18 ANSWER 32 OF 50 CAPLUS COPYRIGHT 2003 ACS  
AN 2001:708596 CAPLUS  
DN 1361116223  
TI Apolipoprotein E and apolipoprotein E receptors modulate  
A.beta.-induced glial neuroinflammatory responses  
AU Iadu, M. J.; Shah, J. A.; Reardon, C. A.; Getz, G. S.; Bu, G.; Hu, J.;  
Guo, L.; Van Eldik, L. J.  
CS Department of Medicine, Evanston Northwestern Healthcare Research  
Institute, Evanston, IL, 60201, USA  
SO Neurochemistry International (2001), 39(5-6), 427-434  
PB Elsevier Science Ltd.  
DT Journal; General Review  
LA English  
RE CNT 61  
THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT



L18 ANSWER 33 OF 50 USPATFULT.  
 AN 2000:102422 USPATFULT.  
 TI Parasitic helminth p22 nucleic acid molecules  
 Tripp, Cynthia Ann, Ft. Collins, CO, United States  
 Frank, Glenn Robert, Ft. Collins, CO, United States  
 Griewe, Robert B., Ft. Collins, CO, United States  
 Heska Corporation, Ft. Collins, CO, United States  
 PA Colorado State University Research Foundation, Ft. Collins, CO, United States (U.S. corporation)  
 PI US 6100390  
 AI US 1995-458860  
 RLI Continuation of Ser. No. US 1993-109391, filed on 19 Aug 1993, now patented, Pat. No. US 5639876 which is a continuation of Ser. No. US 1993-3257, filed on 12 Jan 1993, now abandoned Ser. No. Ser. No. US 1993-3389, filed on 12 Jan 1993, and Ser. No. US 1991-654226, filed on 12 Feb 1991, said Ser. No. US 3257 and Ser. No. US 3389 which is a continuation-in-part of Ser. No. US 654226  
 DT Utility  
 FS Granted  
 INCL INCLM: 536/023.700  
 INCLS: 435/069.100; 435/069.300; 435/071.100; 536/022.100; 536/023.100; 536/024.320  
 NCLM: 536/023.700  
 NCL: 536/023.700  
 NCLS: 435/069.100; 435/069.300; 435/071.100; 536/022.100; 536/023.100; 536/024.320  
 IC [7]  
 ICM: C07H021-04  
 ICS: C07H021-02; C12P021-06; C12P071-04  
 EXP 536/22.1; 536/24.32; 536/23.1; 536/23.7; 435/69.1; 435/69.3; 435/71.1  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 L18 ANSWER 34 OF 50 USPATFULT.  
 AN 2000:102109 USPATFULT.  
 TI O-fucosyltransferase  
 Wang, Yang, Milbrae, CA, United States  
 Spellman, Michael W., Belmont, CA, United States  
 PA Genentech, Inc., South San Francisco, CA, United States (U.S. corporation)  
 PI US 6100076  
 AI US 1997-978741  
 RLI Continuation-in-part of Ser. No. US 1997-792498, filed on 31 Jan 1997, now abandoned  
 DT Utility  
 FS Granted  
 INCL INCLM: 435/193.000  
 INCLS: 435/193.000  
 NCLM: 435/193.000  
 NCL: 435/193.000  
 IC [7]  
 ICM: C12N009-10  
 EXP 435/193  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 L18 ANSWER 35 OF 50 USPATFULT.  
 AN 2000:95093 USPATFULT.  
 TI Isolated peptides derived from the Epstein-Barr virus  
 Barney, Shawn O'lin, Cary, NC, United States  
 Lambert, Dennis Michael, Cary, NC, United States  
 Peteway, Stephen Robert, Cary, NC, United States  
 Trimeris, Inc., Durham, NC, United States (U.S. corporation)  
 PA Duke University, Durham, NC, United States (U.S. corporation)  
 PI US 6093794  
 AI US 1995-471913  
 RLI Division of Ser. No. US 1995-470896, filed on 6 Jun 1995 which is a continuation-in-part of Ser. No. US 1994-360107, filed on 20 Dec 1994

which is a continuation-in-part of Ser. No. US 1994-255208, filed on 7 Jun 1994 which is a continuation-in-part of Ser. No. US 1993-73028, filed on 7 Jun 1993, now patented, Pat. No. US 5464933  
 DT Utility  
 FS Granted  
 INCL INCLM: 530/300.000  
 INCLS: 530/324.000; 530/325.000; 530/326.000; 530/350.000; 424/186.100; 424/230.100  
 NCLM: 530/300.000  
 NCL: 424/186.100; 424/230.100  
 NCLS: 530/350.000  
 IC [7]  
 ICM: A61K038-00  
 ICS: A61K039-12; A61K039-245  
 EXP 530/324; 530/388.3; 530/388.85; 530/389.4; 435/5; 424/147.1; 424/230.1  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 L18 ANSWER 36 OF 50 USPATFULT.  
 AN 2000:67564 USPATFULT.  
 TI Methods for inhibition of membrane fusion-associated events, including influenza virus  
 Barney, Shawn O'lin, Cary, NC, United States  
 Lambert, Dennis Michael, Cary, NC, United States  
 Peteway, Stephen Robert, Cary, NC, United States  
 Trimeris, Inc., Durham, NC, United States (U.S. corporation)  
 PA Duke University, Durham, NC, United States (U.S. corporation)  
 PI US 6068973  
 AI US 1995-485551  
 RLI Division of Ser. No. US 1995-470896, filed on 6 Jun 1995 which is a continuation-in-part of Ser. No. US 1994-360107, filed on 20 Dec 1994 which is a continuation-in-part of Ser. No. US 1994-255208, filed on 7 Jun 1994 which is a continuation-in-part of Ser. No. US 1993-73028, filed on 7 Jun 1993, now patented, Pat. No. US 5464933  
 DT Utility  
 FS Granted  
 INCL INCLM: 435/005.000  
 INCLS: 530/324.000; 530/389.400; 424/147.100; 424/230.100; 424/206.100  
 NCLM: 435/005.000  
 NCL: 424/147.100; 424/206.100; 424/230.100; 530/324.000; 530/389.400  
 IC [7]  
 ICM: C12Q001-70  
 ICS: A61K038-00; A61K039-42; C07K016-00  
 EXP 530/324; 530/389.4; 435/5; 424/147.1; 424/230.1; 424/206.1  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 L18 ANSWER 37 OF 50 USPATFULT.  
 AN 2000:57361 USPATFULT.  
 TI Compositions for inhibition of membrane fusion-associated events, including influenza virus transmission  
 Barney, Shawn O'lin, Cary, NC, United States  
 Lambert, Dennis Michael, Cary, NC, United States  
 Peteway, Stephen Robert, Cary, NC, United States  
 Trimeris, Inc., Durham, NC, United States (U.S. corporation)  
 PA Duke University, Durham, NC, United States (U.S. corporation)  
 PI US 6060065  
 AI US 1995-475668  
 RLI Division of Ser. No. US 1995-470896, filed on 6 Jun 1995 which is a continuation-in-part of Ser. No. US 1994-360107, filed on 20 Dec 1994 which is a continuation-in-part of Ser. No. US 1994-255208, filed on 7 Jun 1994 which is a continuation-in-part of Ser. No. US 1993-73028, filed on 7 Jun 1993, now patented, Pat. No. US 5464933  
 DT Utility  
 FS Granted  
 INCL INCLM: 435/005.000  
 INCLS: 530/324.000; 530/389.400; 424/147.100; 424/230.100; 424/206.100  
 NCLM: 435/005.000  
 NCL: 424/147.100; 424/206.100; 424/230.100; 530/324.000; 530/389.400  
 IC [7]  
 ICM: C12Q001-70  
 ICS: A61K038-00; A61K039-42; C07K016-00  
 EXP 530/324; 530/389.4; 435/5; 424/147.1; 424/230.1; 424/206.1  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 424/209.100  
INCLIS: 424/186.100; 424/192.100; 424/206.100; 530/300.000; 530/324.000;  
530/325.000; 530/326.000; 530/327.000; 530/328.000; 530/329.000;  
530/330.000  
NCL NCLM: 424/209.100  
NCLIS: 424/186.100; 424/192.100; 424/206.100; 530/300.000; 530/324.000;  
530/325.000; 530/326.000; 530/327.000; 530/328.000; 530/329.000;  
530/330.000  
IC [7]  
ICM: A61K039-145  
ICS: A61K039-12; A61K039-00; A61K038-00  
424/209.1; 424/186.1; 424/192.1; 424/206.1; 530/300; 530/324; 530/325;  
530/326; 530/327; 530/328; 530/329; 530/330  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
L18 ANSWER 38 OF 50 USPATFULT  
AN 2000:50515 USPATFULT  
TI Screening assays for compounds that inhibit membrane fusion-associated events  
IN Barney, Shawn O'lin, Cary, NC, United States  
Lambert, Dennis Michael, Cary, NC, United States  
Petteaway, Jr., Stephen Robert, Cary, NC, United States  
Trimeris, Inc., Durham, NC, United States (U.S. corporation)  
PA US 6054265 20000425 (8)  
PI US 1997-919597 19970926 (8)  
RLI Division of Ser. No. US 1995-470896, filed on 6 Jun 1995 which is a continuation-in-part of Ser. No. US 1994-360107, filed on 20 Dec 1994 which is a continuation-in-part of Ser. No. US 1994-255208, filed on 7 Jun 1994 which is a continuation-in-part of Ser. No. US 1993-73028, filed on 7 Jun 1993, now patented, Pat. No. US 5464933  
DT Utility  
FS Granted  
LN.CNT 21307  
INCL INCLM: 435/005.000  
INCLIS: 435/007.200  
NCL NCLM: 435/005.000  
NCLIS: 435/007.200  
IC [7]  
ICM: C120001-70  
EXP 435/5; 435/7.2  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
L18 ANSWER 39 OF 50 USPATFULT  
AN 2000:12922 USPATFULT  
TI Isolated peptides derived from human immunodeficiency virus types 1 and 2 containing fusion inhibitory domains  
IN Barney, Shawn O'lin, Cary, NC, United States  
Lambert, Dennis Michael, Cary, NC, United States  
Petteaway, Jr., Stephen Robert, Cary, NC, United States  
Trimeris, Inc., Durham, NC, United States (U.S. corporation)  
PA US 6020459 20000201  
PI US 1995-484223 19950607 (8)  
RLI Division of Ser. No. US 1995-470896, filed on 6 Jun 1995 which is a continuation-in-part of Ser. No. US 1994-360107, filed on 20 Dec 1994 which is a continuation-in-part of Ser. No. US 1994-255208, filed on 7 Jun 1994 which is a continuation-in-part of Ser. No. US 1993-73028, filed on 7 Jun 1993, now patented, Pat. No. US 5464933  
DT Utility  
FS Granted  
LN.CNT 20335  
INCL INCLM: 530/300.000  
INCLIS: 530/324.000; 530/325.000; 530/326.000; 530/350.000; 424/188.100  
NCL NCLM: 530/300.000  
NCLIS: 530/324.000; 530/325.000; 530/326.000; 530/350.000; 424/188.100  
IC [6]

ICM: A61K038-00  
ICS: A61K039-21  
530/300; 530/317; 530/324  
EXP 530/300; 530/317; 530/324  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
L18 ANSWER 40 OF 50 USPATFULT  
AN 2000:9527 USPATFULT  
TI Simian immunodeficiency virus peptides with antifusogenic and antiviral activities  
IN Barney, Shawn O'lin, Cary, NC, United States  
Lambert, Dennis Michael, Cary, NC, United States  
Petteaway, Jr., Stephen Robert, Cary, NC, United States  
Langlois, Alphonse J., Durham, NC, United States  
Trimeris, Inc., Durham, NC, United States (U.S. corporation)  
PA US 6017536 20000125 (8)  
PI US 1994-360107 19941220 (8)  
RLI Continuation-in-part of Ser. No. US 1994-255208, filed on 7 Jun 1994 which is a continuation-in-part of Ser. No. US 1993-73028, filed on 7 Jun 1993, now patented, Pat. No. US 5464933  
DT Utility  
FS Granted  
LN.CNT 20227  
INCL INCLM: 424/188.100  
INCLIS: 424/208.100; 530/300.000; 530/324.000; 530/325.000; 530/326.000  
NCL NCLM: 424/188.100  
NCLIS: 424/208.100; 530/300.000; 530/324.000; 530/325.000; 530/326.000  
IC [6]  
ICM: A61K039-21  
EXP 530/300; 530/324; 424/184.1; 424/188.1; 424/208.1  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
L18 ANSWER 41 OF 50 USPATFULT  
AN 2000:4427 USPATFULT  
TI Measles virus peptides with antifusogenic and antiviral activities  
IN Barney, Shawn O'lin, Cary, NC, United States  
Lambert, Dennis Michael, Cary, NC, United States  
Petteaway, Jr., Stephen Robert, Cary, NC, United States  
Trimeris, Inc., Durham, NC, United States (U.S. corporation)  
PA US 6013263 20000111  
PI US 1995-486099 19950607 (8)  
RLI Division of Ser. No. US 1995-470896, filed on 6 Jun 1995 which is a continuation-in-part of Ser. No. US 1994-360107, filed on 20 Dec 1994 Ser. No. Ser. No. US 1994-255208, filed on 7 Jun 1994 And Ser. No. US 1993-73028, filed on 7 Jun 1993, now patented, Pat. No. US 5464933  
DT Utility  
FS Granted  
LN.CNT 19827  
INCL INCLM: 424/212.100  
INCLIS: 530/300.000; 530/324.000; 530/325.000; 530/326.000; 424/184.100;  
424/186.100  
NCL NCLM: 424/212.100  
NCLIS: 530/324.000; 424/186.100; 530/300.000; 530/324.000; 530/325.000;  
530/326.000  
IC [6]  
ICM: A61K039-165  
EXP 530/300; 530/324; 424/212.1  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
L18 ANSWER 42 OF 50 CAPLUS COPYRIGHT 2003 ACS  
AN 2000:185820 CAPLUS  
DN 132.306738  
TI Modulation of beta-amyloid precursor protein processing by the low density lipoprotein receptor-related protein (LRP). Evidence that LRP contributes to the pathogenesis of Alzheimer's disease



No. US 1993-3257, filed on 12 Jan 1993, now abandoned Ser. No. Ser. No. US 1993-3389, filed on 12 Jan 1993, now abandoned And Ser. No. US 1991-654226, filed on 12 Feb 1991, now abandoned, said Ser. No. US 3257 which is a continuation-in-part of Ser. No. US 654226, said Ser. No. US 3389 which is a continuation-in-part of Ser. No. US 654226

Utility

DT  
FS  
INCL  
LN.CNT 2357  
INCLM: 536/023.700  
INCLM: 424/184.100; 424/185.100; 424/265.100; 530/350.000; 550/387.100  
NCLM: 536/023.700  
NCLM: 424/184.100; 424/185.100; 424/265.100; 435/007.220; 530/350.000;  
530/387.100  
[6]  
ICM: C07H021-04  
ICS: A61K039-00

EXF  
424/184.1; 424/185.1; 424/265.1; 530/350; 530/300; 550/380; 550/387.1;  
550/388.2; 536/23.7

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L18 ANSWER 48 OF 50 USPATFULT  
AN 97:104113 USPATFULT  
TI Parasitic helminth p4 proteins  
Tripp, Cynthia Ann, Ft. Collins, CO, United States  
Frank, Glenn Robert, Ft. Collins, CO, United States  
Grieve, Robert B., Ft. Collins, CO, United States  
Heska Corporation, Ft. Collins, CO, United States  
Colorado State University Research Foundation, Ft. Collins, CO, United States (U.S. corporation)  
US 5686080  
19971111  
PI US 1995-459019  
AI Continuation of Ser. No. US 1993-109391, filed on 19 Aug 1993, now  
RLI patented, Pat. No. US 5639876 which is a continuation-in-part of Ser.  
No. US 1993-3257, filed on 12 Jan 1993, now abandoned Ser. No. Ser. No.  
US 1993-3389, filed on 12 Jan 1993, now abandoned And Ser. No. US  
1991-654226, filed on 12 Feb 1991, now abandoned, said Ser. No. US  
-3257 And Ser. No. US -3389, each Ser. No. US - which is a  
continuation-in-part of Ser. No. US -654226

DT  
FS  
INCL  
LN.CNT 2279  
INCLM: 424/265.100  
INCLM: 424/154.100; 424/185.100; 424/266.100; 530/350.000; 435/069.100;  
435/069.300; 435/071.100  
NCLM: 424/265.100  
NCLM: 424/184.100; 424/185.100; 424/266.100; 435/069.100; 435/069.300;  
435/071.100; 530/350.000  
[6]  
ICM: A61K039-00  
ICS: A61K039-002; A61K039-38; C07K014-00  
530/350; 530/300; 424/265.1; 424/266.1; 424/184.1; 424/185.1; 435/69.1;  
435/69.3; 435/71.1

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L18 ANSWER 49 OF 50 USPATFULT  
AN 97:52122 USPATFULT  
TI Nucleic acid molecules encoding novel parasitic helminth proteins  
Tripp, Cynthia Ann, Ft. Collins, CO, United States  
Frank, Glenn Robert, Ft. Collins, CO, United States  
Grieve, Robert B., Ft. Collins, CO, United States  
Heska Corporation, Ft. Collins, CO, United States  
Colorado State University Research Foundation, Ft. Collins, CO, United States (U.S. corporation)  
US 5639876  
19970617  
PI US 1993-109391  
AI 19930819 (8)

RLI Continuation-in-part of Ser. No. US 1993-3257, filed on 12 Jan 1993, now  
abandoned Ser. No. Ser. No. US 1993-3389, filed on 12 Jan 1993, now  
abandoned And Ser. No. US 1991-654226, filed on 12 Feb 1991, now  
abandoned, said Ser. No. US -3257 And Ser. No. US -3389, each Ser.  
No. US - which is a continuation-in-part of Ser. No. US -654226

DT  
FS  
INCL  
LN.CNT 2327  
INCLM: 536/023.700  
INCLM: 424/184.100; 424/185.100; 424/265.100; 424/266.100  
NCLM: 536/023.700  
NCLM: 424/184.100; 424/185.100; 424/265.100; 424/266.100; 435/069.100;  
435/069.300; 435/071.100; 536/022.100; 536/023.100  
[6]  
ICM: C07H019-00  
ICS: C07H021-04; C12P021-04; A61K039-00  
536/27; 536/22.1; 536/23.1; 536/23.7; 424/265.1; 424/269.1; 424/184.1;  
424/185.1; 424/165.1; 424/266.1; 435/69.1; 435/69.3; 435/71.1

EXF  
424/185.1; 424/165.1; 424/266.1; 435/69.1; 435/69.3; 435/71.1

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L18 ANSWER 50 OF 50 MEDLINE  
AN 94365030 MEDLINE  
DN 94365030 Pubmed ID: 8083232  
TI The 39-kDa receptor-associated protein regulates ligand binding by the  
very low density lipoprotein receptor.  
Bartley F D; Galvelis M B; Fitzgerald D J; Argaves W S; Chappell D A;  
Straus J F 3rd; Strickland D R  
Holland Laboratory, Department of Biochemistry, American Red Cross,  
Rockville, Maryland 20855.  
CM42581 (NLM) 19941021  
HL49264 (NLM) 19941021  
HL50787 (NLM) 19941011

NC  
CS  
AU  
TI  
DN  
AN  
L18

SO JOURNAL OF BIOLOGICAL CHEMISTRY. (1994 Sep 16) 269 (37) 21268-73.  
+  
CY Journal code: 2985121R. ISSN: 0021-9258.  
DT United States  
LA English  
FS Priority Journals  
EM 199410  
ED Entered STN: 19941021  
Last Updated on STN: 19941021  
Entered Medline: 19941011

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=>  
d his  
(FILE 'HOME' ENTERED AT 15:25:49 ON 20 FEB 2003)  
FILE 'MEDLINE, CANCERLIT, BIOSIS, CONFSCI, EMBASE, CAPUS, USPATFULT'.  
ENTERED AT 15:26:27 ON 20 FEB 2003  
72563 S HEAT (A) SHOCK (A) PROTEIN  
40 S I1 AND ALPHA (A) 2 (A) MACROGLOBULIN (A) RECEPTOR  
33 DUP REM L2 (7 DUPLICATES REMOVED)  
12721 S I1 AND ANTIBODY?  
21 S I4 AND L2  
19 DUP REM L5 (2 DUPLICATES REMOVED)  
1585 S ACONIST? AND L1  
4 S L7 AND L2  
8637 S I1 AND PEPTIDE?  
27 S L9 AND L2  
24 DUP REM L10 (3 DUPLICATES REMOVED)  
11 S L11 AND MODULATE?

L13 1624 S ALPHA (A) 2 (A) MACROGLOBULIN (A) RECEPTOR  
 L14 160 S L13 AND MODULAT?  
 L15 110 DUP REM L14 (50 DUPLICATES REMOVED)  
 L16 14 S L15 AND HEAT (A) SHOCK (A) PROTEIN  
 L17 50 S L14 AND PEPTID?  
 L18 50 DUP REM L17 (0 DUPLICATES REMOVED)  
 L19 => S L14 and antibody?  
 71 L14 AND ANTIBOD?  
 => dup rem l19  
 PROCESSING COMPLETED FOR L19  
 L20 60 DUP REM L19 (11 DUPLICATES REMOVED)  
 => d 120 not py=>2000  
 'NOT' IS NOT A VALID FORMAT  
 In a multifile environment, a format can only be used if it is valid  
 in at least one of the files. Refer to file specific help messages  
 or the STNGUIDE file for information on formats available in  
 individual files.  
 REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):exit  
 'EXIT' IS NOT A VALID FORMAT  
 In a multifile environment, a format can only be used if it is valid  
 in at least one of the files. Refer to file specific help messages  
 or the STNGUIDE file for information on formats available in  
 individual files.  
 REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):bye  
 'BYE' IS NOT A VALID FORMAT  
 In a multifile environment, a format can only be used if it is valid  
 in at least one of the files. Refer to file specific help messages  
 or the STNGUIDE file for information on formats available in  
 individual files.  
 REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):stop  
 'STOP' IS NOT A VALID FORMAT  
 In a multifile environment, a format can only be used if it is valid  
 in at least one of the files. Refer to file specific help messages  
 or the STNGUIDE file for information on formats available in  
 individual files.  
 REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):end  
 => S 120 not py=>2000  
 '2000' NOT A VALID FIELD CODE  
 L21 13 L20 NOT PY=>2000  
 => d 1-13  
 L21 ANSWER 1 OF 13 MEDLINE  
 AN 9715686 MEDLINE  
 DN 9715686 Pubmed ID: 9003247  
 TI Modulation of the alpha 2  
 macroglobulin receptor/low density lipoprotein receptor  
 related protein by interferon-gamma in human astroglial cells.  
 AU Bushnoro R; Fabrizio C; Persichini T; Starace G; Ennas M G; Fumagalli L;  
 Lauro G M  
 CS Dipartimento di Scienze Cardiovascolari e Respiratorie, Universita La  
 Sapienza, Rome, Italy.  
 SO JOURNAL OF NEUROIMMUNOLOGY. (1997 Jan) 72 (1). 75-81.  
 CY Journal code: 8109498. ISSN: 0165-5728.  
 NC Netherlands  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 OS GENBANK-X55077  
 EM 199702  
 ED Entered STN: 19970305

Last Updated on STN: 19970305  
 Entered Medline: 19970219  
 L21 ANSWER 2 OF 13 MEDLINE  
 AN 95072001 MEDLINE  
 DN 95072001 Pubmed ID: 7526898  
 TI Presence of LDL receptor-related protein/alpha 2-  
 macroglobulin receptors in macrophages of  
 atherosclerotic lesions from cholesterol-fed New Zealand and heterozygous  
 Metanabe heritable hyperlipidemic rabbits.  
 AU Daugherty A; Rateri D L  
 CS Cardiovascular Division, Washington University School of Medicine, St.  
 Louis, MO 63110.  
 NC HT-17646 (NHLBI)  
 SO ARTERIOSCLEROSIS AND THROMBOSIS. (1994 Dec) 14 (12) 2017-24.  
 CY Journal code: 9101386. ISSN: 1049-8834.  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 199412  
 ED Entered STN: 19950116  
 Last Updated on STN: 19960129  
 Entered Medline: 19941230  
 L21 ANSWER 3 OF 13 MEDLINE  
 AN 9414468 MEDLINE  
 DN 9414468 Pubmed ID: 7508685  
 TI Expression of alpha 2-macroglobulin  
 receptor/low density lipoprotein receptor-related protein and the  
 39-kd receptor-associated protein in human trophoblasts.  
 AU Coukos G; Gafvels M E; Wisel S; Ruelaz E A; Strickland D K; Straus J F  
 3rd; Coutifaris C  
 CS Department of Obstetrics and Gynecology, University of Pennsylvania School  
 of Medicine, Philadelphia.  
 NC CM-42581 (NIGMS)  
 SO AMERICAN JOURNAL OF PATHOLOGY. (1994 Feb) 144 (2) 383-92.  
 CY Journal code: 0370502. ISSN: 0002-9440.  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Abridged Index Medicus Journals; Priority Journals  
 EM 199403  
 ED Entered STN: 19940330  
 Last Updated on STN: 19960129  
 Entered Medline: 19940317  
 L21 ANSWER 4 OF 13 MEDLINE  
 AN 92366474 MEDLINE  
 DN 92366474 Pubmed ID: 1502154  
 TI Low density lipoprotein receptor-related protein/alpha 2  
 -macroglobulin receptor is an hepatic receptor for  
 tissue-type plasminogen activator.  
 AU Bu G; Williams S; Strickland D K; Schwartz A L  
 CS Edward Mallinckrodt Department of Pediatrics, Washington University School  
 of Medicine, St. Louis, MO 63110.  
 NC H108467 (NHLBI)  
 SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF  
 AMERICA. (1992 Aug 15) 89 (16) 7427-31.  
 CY Journal code: 7505876. ISSN: 0027-8424.  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English

FS Priority Journals  
 EM 199209  
 Entered STN: 19920925  
 Last Updated on STN: 19980206  
 Entered Medicine: 19920915

L21 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2003 ACS  
 AN 1999:180032 CAPLUS  
 DN 13:11513  
 TI Do P-glycoprotein and major vault protein (MVP/LMP) expression correlate with in vitro daunorubicin resistance in acute myeloid leukemia?  
 AU Broxmeyer, H. J.; Sonnewald, P.; Pieciers, R.; Lankester, J.; Bekman, C. A.; Looijen, A. H.; Schoester, M.; Ossenkoppele, G. J.; Lowenberg, B.; Pinedo, H. M.; Schuurhuis, G. J.  
 CS Department of Medical Oncology, University Hospital Vrije Universiteit, Amsterdam, 1007 MB, Neth.  
 SO Leukemia (1999), 13(2), 258-265  
 CODEN: LEUKED; ISSN: 0887-6624  
 PB Stockton Press  
 DT Journal  
 LA English  
 RE.CNT 34

THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2003 ACS  
 AN 1997:188130 CAPLUS  
 DN 126:275326  
 TI Low density lipoprotein receptor-related protein modulates the expression of tissue-type plasminogen activator in human colon fibroblasts  
 AU Hardy, Medora M.; Feder, Joseph; Wolfe, Richard A.; Bu, Guojun  
 CS Dep. of Cell Culture and Biochemistry, Monsanto Co., St. Louis, MO, 63167, USA  
 SO Journal of Biological Chemistry (1997), 272(10), 6812-6817  
 CODEN: JBCHA3; ISSN: 0021-9258  
 PB American Society for Biochemistry and Molecular Biology  
 DT Journal  
 LA English

L21 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2003 ACS  
 AN 1997:82858 CAPLUS  
 DN 126:169578  
 TI The low-density lipoprotein receptor-related protein, a multifunctional apolipoprotein E receptor, modulates hippocampal neurite development  
 AU Naita, Masaaki; Bu, Guojun; Holtzman, David M.; Schwartz, Alan L.  
 CS Department of Pediatrics, Washington University School of Medicine, St. Louis, MO, 63110, USA  
 SO Journal of Neurochemistry (1997), 68(2), 587-595  
 CODEN: JONRA9; ISSN: 0022-3042  
 PB Lippincott-Raven  
 DT Journal  
 LA English

L21 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2003 ACS  
 AN 1996:717281 CAPLUS  
 DN 126:29495  
 TI Apolipoprotein E-containing high density lipoprotein promotes neurite outgrowth and is a ligand for the low density lipoprotein receptor-related protein  
 AU Fagan, Anne M.; Bu, Guojun; Sun, Yuling; Daugherty, Alan; Holtzman, David M.  
 CS Dep. Neurology, Washington Univ. School Medicine, St. Louis, MO, 63110, USA  
 SO Journal of Biological Chemistry (1996), 271(47), 30121-30125  
 CODEN: JBCHA3; ISSN: 0021-9258

PB American Society for Biochemistry and Molecular Biology  
 DT Journal  
 LA English

L21 ANSWER 9 OF 13 USPATFILL  
 AN 1999:141305 USPATFILL  
 TI Adjuvant for transcutaneous immunization  
 AU Glenn, Gregory M.; Bethesda, MD, United States  
 IN Alving, Carl R.; Bethesda, MD, United States  
 PA The United States of America as represented by the U.S. Army Medical Research & Materiel Command, Washington, DC, United States (U.S. government)  
 PI US 5980898  
 AI US 1997-896085  
 RLI Continuation-in-part of Ser. No. US 1996-749164, filed on 14 Nov 1996  
 DT Utility  
 PS Granted  
 IN.CNT 1988  
 INCL INCL: 424/184.100  
 INCL: 424/449.000; 424/450.000; 424/236.000; 424/240.100; 424/241.100; 424/275.100; 530/363.000; 530/403.000  
 NCL NCLM: 424/184.100  
 NCL: 424/085.100; 424/240.100; 424/241.100; 424/275.100; 424/449.000; 424/450.000; 530/363.000; 530/403.000  
 IC [6]  
 ICM: A61K039-00  
 ICS: C07K014-005; C07K014-195  
 EXF 424/449; 424/450; 424/184.1; 424/236; 424/240.1; 424/241.1; 424/275.1; 530/363; 530/403  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L21 ANSWER 10 OF 13 USPATFILL  
 AN 1999:67356 USPATFILL  
 TI Parasitic helminth p220 proteins  
 IN Tripp, Cynthia Ann, Ft. Collins, CO, United States  
 PA Frank, Glenn Robert, Ft. Collins, CO, United States  
 PA Greive, Robert B., Ft. Collins, CO, United States  
 PA Heesla Corporation, Ft. Collins, CO, United States (U.S. corporation)  
 PA Colorado State University Research Foundation, Ft. Collins, CO, United States (U.S. corporation)  
 PI US 5912337  
 AI US 1995-460428  
 RLI Continuation of Ser. No. US 1993-109391, filed on 19 Aug 1993, now patented, Pat. No. US 5639876 which is a continuation-in-part of Ser. No. US 1993-3257, filed on 12 Jan 1993, now abandoned Ser. No. US 1993-3389, filed on 12 Jan 1993, now abandoned and Ser. No. US 3257 1991-654226, filed on 12 Feb 1991, now abandoned, said Ser. No. US 3257 which is a continuation-in-part of Ser. No. US 654226, said Ser. No. US 3389 which is a continuation-in-part of Ser. No. US 654226  
 DT Utility  
 PS Granted  
 IN.CNT 2357  
 INCL INCLM: 536/023.700  
 INCL: 424/184.100; 424/185.100; 424/265.100; 530/350.000; 550/387.100  
 NCL NCLM: 536/023.700  
 NCL: 424/184.100; 424/185.100; 424/265.100; 435/007.220; 530/350.000; 530/387.100  
 IC [6]  
 ICM: C07H021-04  
 ICS: A61K039-00  
 EXF 424/184.1; 424/185.1; 424/265.1; 530/350; 530/380; 550/387.1; 550/388.2; 536/23.7  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L21 ANSWER 11 OF 13 USPATFILL

AN 1998:30893 USPTAFULL  
 TI Non-mammalian DNA virus to express an exogenous gene in a mammalian cell  
 IN Boyce, Frederick M., Belmont, MA, United States  
 PA The General Hospital Corporation, Boston, MA, United States (U.S. corporation)  
 PI US 5731182 19980124  
 AI US 1995-486341 19950607 (8)  
 RLI Continuation-in-part of Ser. No. US 1994-311157, filed on 23 Sep 1994  
 DT Utility  
 FS Granted  
 LN.CNT 1730  
 INCL INCLM: 435/183.000  
 INCLS: 435/320.100; 435/069.100; 435/070.100  
 NCLM: 435/183.000  
 NCLS: 435/069.100; 435/070.100; 435/320.100  
 IC [6]  
 ICM: C12N009-00  
 ICS: C12N015-63; C12P021-02  
 EXP 435/183; 435/1837; 435/320.1; 435/69.1; 435/70.1  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L21 ANSWER 12 OF 13 USPTAFULL  
 AN 97:104113 USPTAFULL  
 TI Parasitic helminth p4 proteins  
 IN Tripp, Cynthia Ann, Ft. Collins, CO, United States  
 PA Frank, Glenn Robert, Ft. Collins, CO, United States  
 PI US 5686080 19971111  
 AI US 1995-459019 19950602 (8)  
 RLI Continuation of Ser. No. US 1993-109391, filed on 19 Aug 1993, now patented, Pat. No. US 5639876 which is a continuation-in-part of Ser. No. US 1993-3257, filed on 12 Jan 1993, now abandoned and Ser. No. US 1993-3389, filed on 12 Jan 1993, now abandoned and Ser. No. US 1991-654226, filed on 12 Feb 1991, now abandoned, said Ser. No. US -3257 and Ser. No. US -3389, each Ser. No. US - which is a continuation-in-part of Ser. No. US -654226  
 DT Utility  
 FS Granted  
 LN.CNT 2279  
 INCL INCLM: 424/265.100  
 INCLS: 424/154.100; 424/185.100; 424/266.100; 530/350.000; 435/069.100; 435/069.300; 435/071.100  
 NCLM: 424/265.100  
 NCLS: 424/184.100; 424/185.100; 424/266.100; 435/069.100; 435/069.300; 435/071.100; 530/350.000  
 IC [6]  
 ICM: A61K039-00  
 ICS: A61K039-002; A61K039-38; C07K014-00  
 EXP 530/350; 530/300; 424/265.1; 424/266.1; 424/184.1; 424/185.1; 435/69.1; 435/69.3; 435/71.1  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L21 ANSWER 13 OF 13 USPTAFULL  
 AN 97:52122 USPTAFULL  
 TI Nucleic acid molecules encoding novel parasitic helminth proteins  
 IN Tripp, Cynthia Ann, Ft. Collins, CO, United States  
 PA Frank, Glenn Robert, Ft. Collins, CO, United States  
 PI US 5639876 19970617

AI US 1993-109391 19930819 (8)  
 RLI Continuation-in-part of Ser. No. US 1993-3257, filed on 12 Jan 1993, now abandoned and Ser. No. US 1993-3389, filed on 12 Jan 1993, now abandoned and Ser. No. US 1991-654226, filed on 12 Feb 1991, now abandoned, said Ser. No. US -3257 and Ser. No. US -3389, each Ser. No. US - which is a continuation-in-part of Ser. No. US -654226  
 DT Utility  
 FS Granted  
 LN.CNT 2327  
 INCL INCLM: 536/023.700  
 INCLS: 536/022.100; 536/023.100; 435/069.100; 435/069.300; 435/071.100; 424/184.100; 424/185.100; 424/265.100; 424/266.100  
 NCLM: 536/023.700  
 NCLS: 424/184.100; 424/185.100; 424/265.100; 424/266.100; 435/069.100; 435/069.300; 435/071.100; 536/022.100; 536/023.100  
 IC [6]  
 ICM: C07H019-00  
 ICS: C07H021-04; C12P021-04; A61K039-00  
 EXP 536/27; 536/22.1; 536/23.1; 536/23.7; 424/265.1; 424/269.1; 424/184.1; 424/185.1; 424/165.1; 424/266.1; 435/69.1; 435/69.3; 435/71.1  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d his  
 (FILE 'HOME' ENTERED AT 15:25:49 ON 20 FEB 2003)  
 FILE 'MEDLINE, CANCERLIT, BIOSIS, CONFSCI, EMBASE, CAPLUS, USPTAFULL'  
 ENTERED AT 15:26:27 ON 20 FEB 2003  
 L1 7563 S HEAT (A) SHOCK (A) PROTEIN  
 L2 40 S L1 AND ALPHA (A) 2 (A) MACROGLOBULIN (A) RECEPTOR  
 L3 33 DUP REM L2 (7 DUPLICATES REMOVED)  
 L4 12721 S L1 AND ANTIBODY?  
 L5 21 S L4 AND L2  
 L6 19 DUP REM L5 (2 DUPLICATES REMOVED)  
 L7 1585 S AGONIST? AND L1  
 L8 4 S L7 AND L2  
 L9 8637 S L1 AND PEPTIDE?  
 L10 27 S L9 AND L2  
 L11 24 DUP REM L10 (3 DUPLICATES REMOVED)  
 L12 11 S L11 AND MODULATE?  
 L13 1624 S ALPHA (A) 2 (A) MACROGLOBULIN (A) RECEPTOR  
 L14 160 S L13 AND MODULATE?  
 L15 110 DUP REM L14 (50 DUPLICATES REMOVED)  
 L16 14 S L15 AND HEAT (A) SHOCK (A) PROTEIN  
 L17 50 S L14 AND PEPTID?  
 L18 50 DUP REM L17 (0 DUPLICATES REMOVED)  
 L19 71 S L14 AND ANTIBODY?  
 L20 60 DUP REM L19 (11 DUPLICATES REMOVED)  
 L21 13 S L20 NOT PY=>2000

=> s l14 and TPA  
 L22 7 L14 AND TPA

=> d 1-7  
 L22 ANSWER 1 OF 7 USPTAFULL  
 AN 2003:37187 USPTAFULL  
 TI Anticolic liposomes for delivery of bioactive agents  
 IN Lakkaraju, Aparna, Minneapolis, MN, UNITED STATES  
 PI Dubinsky, Janet M., St. Paul, MN, UNITED STATES  
 PA Low, Walter, Shorewood, MN, UNITED STATES  
 PI Rahman, Yueh-Erh, LaJolla, CA, UNITED STATES  
 AI US 2003026831 A1 20030206  
 PI US 2002-131786 A1 20020422 (10)

PRAI US 2001-285337P 20010420 (60)  
 DT Utility  
 FS APPLICATION  
 LN.CNT 3617  
 INCL INCLM: 424/450.000  
 NCL NCLM: 424/450.000  
 IC [7]  
 ICM: A61K009-127  
  
 L22 ANSWER 2 OF 7 USPTAFULL  
 AN 2003:30238 USPTAFULL  
 TI Secreted protein HLHP03  
 IN Fischer, Carrie L., Burke, VA, UNITED STATES  
 Rosen, Craig A., Laytonville, MD, UNITED STATES  
 Soppet, Daniel R., Centerville, VA, UNITED STATES  
 Ruben, Steven M., Olney, MD, UNITED STATES  
 Kyaw, Hla, Frederick, CA, UNITED STATES  
 Li, Yi, Sunnyvale, CA, UNITED STATES  
 Zeng, Zhizhen, Lansdale, PA, UNITED STATES  
 Lafleur, David W., Washington, DC, UNITED STATES  
 Moore, Paul A., Germantown, MD, UNITED STATES  
 Shi, Yangu, Gaithersburg, MD, UNITED STATES  
 Olsen, Henrik S., Gaithersburg, MD, UNITED STATES  
 Ebner, Reinhard, Gaithersburg, MD, UNITED STATES  
 Brewer, Laurie A., St. Paul, MN, UNITED STATES  
 PI US 2001-983802 AI 20030130  
 AI 2001025 (9)  
 RLI Continuation of Ser. No. US 1999-227357, filed on 8 Jan 1999, GRANTED,  
 Pat. No. US 6342581 Continuation-in-part of Ser. No. WO 1998-US13684,  
 filed on 7 Jul 1998, UNKNOWN  
 PRAI US 1997-51926P 19970708 (60)  
 US 1997-52793P 19970708 (60)  
 US 1997-51925P 19970708 (60)  
 US 1997-51929P 19970708 (60)  
 US 1997-52803P 19970708 (60)  
 US 1997-52732P 19970708 (60)  
 US 1997-51931P 19970708 (60)  
 US 1997-51932P 19970708 (60)  
 US 1997-51916P 19970708 (60)  
 US 1997-51930P 19970708 (60)  
 US 1997-51918P 19970708 (60)  
 US 1997-51920P 19970708 (60)  
 US 1997-52733P 19970708 (60)  
 US 1997-52795P 19970708 (60)  
 US 1997-51919P 19970708 (60)  
 US 1997-51928P 19970708 (60)  
 US 1997-55722P 19970818 (60)  
 US 1997-55723P 19970818 (60)  
 US 1997-55948P 19970818 (60)  
 US 1997-55949P 19970818 (60)  
 US 1997-55953P 19970818 (60)  
 US 1997-55950P 19970818 (60)  
 US 1997-55947P 19970818 (60)  
 US 1997-55964P 19970818 (60)  
 US 1997-56160P 19970818 (60)  
 US 1997-55684P 19970818 (60)  
 US 1997-55984P 19970818 (60)  
 US 1997-55954P 19970912 (60)  
 US 1997-58785P 19970912 (60)  
 US 1997-58664P 19970912 (60)  
 US 1997-58660P 19970912 (60)  
 US 1997-58661P 19970912 (60)  
 DT Utility  
 FS APPLICATION  
 LN.CNT 19390

INCL INCLM: 435/006.000  
 INCLS: 435/069.100; 435/325.000; 435/320.100; 435/183.000; 536/023.200  
 NCL NCLM: 435/006.000  
 NCLS: 435/069.100; 435/325.000; 435/320.100; 435/183.000; 536/023.200  
 IC [7]  
 ICM: C12Q001-68  
 ICS: C07H021-04; C12N009-00; C12P021-02; C12N005-06  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
  
 L22 ANSWER 3 OF 7 USPTAFULL  
 AN 2002:19393 USPTAFULL  
 TI Secreted protein HLHP03  
 IN Rosen, Craig A., Laytonville, MD, United States  
 Ruben, Steven M., Olney, MD, United States  
 Olsen, Henrik S., Gaithersburg, MD, United States  
 Ebner, Reinhard, Gaithersburg, MD, United States  
 Human Genome Sciences, Inc., Rockville, MD, United States (U.S. corporation)  
 PA  
 PI US 6342581 BI 20020129  
 AI US 1999-227357 19990108 (9)  
 RLI Continuation-in-part of Ser. No. WO 1998-US13684, filed on 7 Jul 1998  
 PRAI US 1997-58785P 19970912 (60)  
 US 1997-58664P 19970912 (60)  
 US 1997-58660P 19970912 (60)  
 US 1997-58661P 19970912 (60)  
 US 1997-55722P 19970818 (60)  
 US 1997-55723P 19970818 (60)  
 US 1997-55948P 19970818 (60)  
 US 1997-55949P 19970818 (60)  
 US 1997-55953P 19970818 (60)  
 US 1997-55950P 19970818 (60)  
 US 1997-55947P 19970818 (60)  
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 US 1997-56160P 19970818 (60)  
 US 1997-55684P 19970818 (60)  
 US 1997-55984P 19970818 (60)  
 US 1997-55954P 19970818 (60)  
 US 1997-51926P 19970708 (60)  
 US 1997-52793P 19970708 (60)  
 US 1997-51925P 19970708 (60)  
 US 1997-51929P 19970708 (60)  
 US 1997-51920P 19970708 (60)  
 US 1997-52803P 19970708 (60)  
 US 1997-52732P 19970708 (60)  
 US 1997-51931P 19970708 (60)  
 US 1997-51932P 19970708 (60)  
 US 1997-51916P 19970708 (60)  
 US 1997-51930P 19970708 (60)  
 US 1997-51918P 19970708 (60)  
 US 1997-51920P 19970708 (60)  
 US 1997-52733P 19970708 (60)  
 US 1997-52795P 19970708 (60)  
 US 1997-51919P 19970708 (60)  
 US 1997-51928P 19970708 (60)  
 DT Utility  
 FS GRANTED  
 LN.CNT 18742  
 INCL INCLM: 530/300.000  
 INCLS: 530/350.000; 435/069.100  
 NCL NCLM: 530/300.000  
 NCLS: 435/069.100; 530/350.000  
 IC [7]  
 ICM: A61K038-00  
 ICS: C07K001-00; C12P021-06  
 EXF 530/300; 530/350; 435/69.1  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.



L22 ANSWER 4 OF 7 USPTAFULL  
 AN 2001:18654 USPTAFULL  
 TI Suppression of inhibitors  
 IN Brunner, Nils, Vitum, Denmark  
 Rømer, John, Copenhagen, Denmark  
 Ellis, Vincent, Woodford Green, Great Britain  
 Pyke, Charles, Copenhagen, Denmark  
 Grondahl-Hansen, Jan, Holte, Denmark  
 Pappot, Helle Pedersen, Allerød, Denmark  
 Hansen, Heine Høi, Holte, Denmark  
 Dano, Keld, Charlottelund, Denmark  
 PI US 2001034327 AI 20010418 (9)  
 AI US 2001-836323 AI 20010418 (9)  
 RLI Division of Ser. No. US 1996-583129, filed on 15 May 1996, GRANTED, Pat.  
 No. US 6224665 A 371 of International Ser. No. WO 1994-DK288, filed on  
 18 Jul 1994, UNKNOWN 19930716  
 PRAI DK 1993-851  
 DT Utility  
 FS APPLICATION  
 LN CNT 2247  
 INCL INCLM: 514/012.000  
 INCLM: 435/007.230  
 NCLM: 514/012.000  
 NCL NCLM: 435/007.230  
 IC [7]  
 ICM: G01N033-574  
 ICS: A61K038-55  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L22 ANSWER 5 OF 7 USPTAFULL  
 AN 2001:125760 USPTAFULL  
 TI O-fucosyltransferase  
 IN Wang, Yang, Milbrase, CA, United States  
 Spellman, Michael W., Belmont, CA, United States  
 Genentech, Inc., South San Francisco, CA, United States (U.S.  
 corporation)  
 PI US 6270987 B1 20010807  
 AI US 1999-333729 19990615 (9)  
 RLI Division of Ser. No. US 1997-978741, filed on 26 Nov 1997, now patented,  
 Pat. No. US 6100076, issued on 8 Aug 2000 Continuation-in-part of Ser.  
 No. US 1997-792498, filed on 31 Jan 1997, now abandoned  
 DT Utility  
 FS GRANTED  
 LN CNT 3080  
 INCL INCLM: 435/068.100  
 INCLM: 435/015.000; 435/053.000; 435/041.000; 435/072.000; 435/097.000;  
 NCLM: 435/193.000; 435/200.000  
 NCLM: 435/068.100  
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 ICS: C12N009-10  
 EXP 435/15; 435/68.1; 435/53; 435/41; 435/72; 435/97; 435/193; 435/200  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L22 ANSWER 6 OF 7 USPTAFULL  
 AN 2001:63243 USPTAFULL  
 TI Suppression of inhibitors  
 IN Brunner, Nils, Hellerup, Denmark  
 Rømer, John, Copenhagen, Denmark  
 Ellis, Vincent, Woodford Green, United Kingdom  
 Pyke, Charles, Allerød, Denmark  
 Grøndahl-Hansen, Jan, Holte, Denmark  
 Grøndahl-Hansen, Jan, Holte, Denmark

PA Pedersen, Helle, Allerød, Denmark  
 Hansen, Heine Høi, Holte, Denmark  
 Dano, Keld, Charlottelund, Denmark  
 Cancerforskningsfonden AF 1989, Copenhagen K, Denmark (non-U.S.  
 corporation)  
 PI US 624865 B1 20010501  
 AI WO 9502413 19950126  
 AI US 1996-583129 19960515 (8)  
 WO 1994-DK288 19940718  
 PRAI DK 1993-851 19930716  
 DT Utility  
 FS Granted  
 LN CNT 2471  
 INCL INCLM: 424/130.100  
 INCLM: 421/138.100; 421/141.100; 421/145.100; 421/155.100; 421/157.100;  
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 NCLM: 424/130.100  
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 ICS: A01N037-18  
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 424/158.1; 424/172.1; 424/179.1; 424/181.1; 424/183.1; 514/2  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L22 ANSWER 7 OF 7 USPTAFULL  
 AN 2000:102109 USPTAFULL  
 TI O-fucosyltransferase  
 IN Wang, Yang, Milbrase, CA, United States  
 Spellman, Michael W., Belmont, CA, United States  
 Genentech, Inc., South San Francisco, CA, United States (U.S.  
 corporation)  
 PI US 6100076 20000808  
 AI US 1997-978741 19971126 (8)  
 RLI Continuation-in-part of Ser. No. US 1997-792498, filed on 31 Jan 1997,  
 now abandoned  
 DT Utility  
 FS Granted  
 LN CNT 3438  
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SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1992 Aug 15) 89 (16) 7427-31.  
Journal code: 7505876. ISSN: 0027-8424.

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DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
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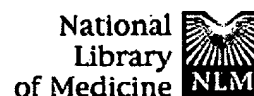
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L24 ANSWER 5 OF 7 USPATFULL  
AN 2001:63243 USPATFULL  
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R.O. slashed mer. John, Copenhagen, Denmark  
Ellis, Vincent, Woodford Green, United Kingdom  
Pyke, Charles, Hillerød slashed.d, Denmark  
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Pedersen, Helene, Allerød slashed.d, Denmark  
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Dan.O slashed. , Keld, Charlottenlund, Denmark  
Cancerforskningsfonden AF 1989, Copenhagen K, Denmark (non-U.S.  
corporation)  
PA US 6224865 B1 20010501  
PI WO 9502413 19950126  
AI US 1996-583129 19960515 (8)  
WO 1994-DK288 19940718  
19960515 PCT 371 date  
19960515 PCT 102(e) date  
19930716  
PRAI DK 1993-851  
DT Utility  
FS Granted  
LN.CNT 2471  
INCL INCLM: 424/130.100  
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514/002.000  
NCLM: 424/130.100  
NCLS: 424/138.100; 424/141.100; 424/145.100; 424/152.100; 424/155.100;  
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514/002.000  
IC [7]  
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ICS: A01N037-18  
EXF 424/152.1: 424/141.1; 424/145.1; 424/155.1; 424/130.1; 424/138.1;  
424/158.1; 424/172.1; 424/179.1; 424/181.1; 424/183.1; 514/2  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
L24 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2003 ACS  
AN 1997:188130 CAPLUS  
DN 126:275326  
TI Low density lipoprotein receptor-related protein modulates the  
expression of tissue-type plasminogen  
activator in human colon fibroblasts  
AU Hardy, Medora M.; Feder, Joseph; Wolfe, Richard A.; Bu, Guojun  
CS Dep. of Cell Culture and Biochemistry, Monsanto Co., St. Louis, MO. 63167,  
USA  
SO Journal of Biological Chemistry (1997), 272(10), 6812-6817  
CODEN: JBCHA3; ISSN: 0021-9258  
PB American Society for Biochemistry and Molecular Biology  
DT Journal  
LA English  
L24 ANSWER 7 OF 7 MEDLINE  
AN 92366474 MEDLINE  
DN 92366474 PubMed ID: 1502154  
TI Low density lipoprotein receptor-related protein/alpha 2  
-macroglobulin receptor is an hepatic receptor for  
tissue-type plasminogen activator.  
AU Bu G; Williams S; Strickland D K; Schwartz A L  
CS Edward Mallinckrodt Department of Pediatrics, Washington University School  
of Medicine, St. Louis, MO 63110.  
NC HL08467 (NHLBI)  
HL17646 (NHLBI)



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**ELSEVIER SCIENCE  
FULL-TEXT ARTICLE****Characterization of the soluble form of the low density lipoprotein receptor-related protein (LRP).****Quinn KA, Pye VJ, Dai YP, Chesterman CN, Owensby DA.**

Centre for Thrombosis and Vascular Research, School of Pathology, Kensington, New South Wales, 2052, Australia. k.quinn@unsw.edu.au

We report characterization of the soluble form of the low density lipoprotein receptor-related protein (sLRP) which circulates in human plasma. Amino acid sequence analysis confirmed that sLRP isolated from human plasma contains the alpha-chain of LRP1. In addition, Western blot analysis identified a truncated beta-chain noncovalently associated with the purified alpha-chain. The molecular size (M(r) 55K) of the peptide portion of the truncated beta-chain indicates that the subunit comprises the extracellular portion of the beta-chain and terminates in a membrane-proximal region. We investigated the mechanism by which sLRP may be generated using the trophoblast cell line, BeWo, which releases sLRP in culture. Cell surface labeling experiments indicate that LRP is released from BeWo cells following expression at the cell surface. Incubation of BeWo cells in the presence of a metalloproteinase inhibitor, INH-3855-PI, results in a dose-dependent inhibition of LRP shedding. The metalloproteinase responsible for the shedding of LRP by BeWo cells is not up-regulated by phorbol ester and is not dependent on serine proteases, such as plasmin, for activity. The BeWo cell line is derived from a human gestational choriocarcinoma and preliminary studies suggest that LRP may be shed within the placenta during gestation. Increased levels of sLRP were detected in cord blood. In term placenta, LRP is expressed in the syncytium, which comprises the maternal-fetal interface. Increased levels of sLRP in cord blood may reflect cellular dysfunction and increased metalloproteinase activity at this important interface. Copyright 1999 Academic Press.

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Abstract



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**FREE full text article at  
circ.ahajournals.org****Antagonists of the mannose receptor and the LDL receptor-related protein dramatically delay the clearance of tissue plasminogen activator.****Biessen EA, van Teijlingen M, Vietsch H, Barrett-Bergshoeff MM, Bijsterbosch MK, Rijken DC, van Berkel TJ, Kuiper J.**

Division of Biopharmaceutics, Leiden/Amsterdam Center for Drug Research, University of Leiden, The Netherlands.

**BACKGROUND:** Clinical application of tissue plasminogen activator (TPA) as a fibrinolytic agent is complicated by its rapid clearance from the bloodstream, which is caused by TPA liver uptake. The mannose receptor on endothelial liver cells and the LDL receptor-related protein (LRP) on parenchymal liver cells were reported to contribute to liver uptake. **METHODS AND RESULTS:** In this study, we addressed whether TPA clearance can be delayed by inhibiting receptor-mediated endocytosis of TPA. A series of cluster mannosides was synthesized, and their affinity for the mannose receptor was determined. A cluster mannoside carrying six mannose groups (M6L5) displayed a subnanomolar affinity for the mannose receptor ( $K_i = 0.41 \pm 0.09$  nmol/L). Preinjection of M6L5 (1.2 mg/kg) reduced the clearance of  $^{125}\text{I}$ -TPA in rats by 60% because of specific inhibition of the endothelial cell uptake. The low toxicity of M6L5, combined with its accessible synthesis and high specificity for the mannose receptor, makes it a promising agent to improve the pharmacokinetics of TPA. Blockade of LRP by 39-kD receptor-associated protein (GST-RAP) also inhibited TPA clearance by 60%. Finally, combined preinjection of M6L5 and GST-RAP almost completely abolished reduced liver uptake of TPA and delayed its clearance by a factor of 10. **CONCLUSIONS:** It can be concluded that (1) the mannose receptor and LRP appear to be the sole major receptors responsible for TPA clearance and (2) therapeutic levels of TPA can be maintained for a prolonged time span by coadministration of the aforementioned receptor antagonists.

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# Circulation

(Circulation. 1997;95:46-52.)

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## Articles

### Antagonists of the Mannose Receptor and the LDL Receptor-Related Protein Dramatically Delay the Clearance of Tissue Plasminogen Activator

Erik A.L. Biessen, PhD; Marco van Teijlingen; Helene Vietsch; Marrie M. Barrett-Bergshoeff; Martin K. Bijsterbosch, PhD; Dingeman C. Rijken, PhD; Theo J.C. van Berkel, PhD; Johan Kuiper, PhD

the Division of Biopharmaceutics, Leiden/Amsterdam Center for Drug Research, University of Leiden (E.A.L.B., M.v.T., H.V., M.K.B., T.J.C.v.B., J.K.), and Gaubius Laboratory, TNO Prevention and Health (M.M.B.-B., D.C.R.), Leiden, The Netherlands.

Correspondence to Dr Ir E.A.L. Biessen, Division of Biopharmaceutics, LACDR, University of Leiden, PO Box 9503, 2300 RA Leiden, The Netherlands.

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## ► Abstract

**Background** Clinical application of tissue plasminogen activator (TPA) as a fibrinolytic agent is complicated by its rapid clearance from the bloodstream, which is caused by TPA liver uptake. The mannose receptor on endothelial liver cells and the LDL receptor-related protein (LRP) on parenchymal liver cells were reported to contribute to liver uptake.

**Methods and Results** In this study, we addressed whether TPA clearance can be delayed by inhibiting receptor-mediated endocytosis of TPA. A series of cluster mannosides was synthesized, and their affinity for the mannose receptor was determined. A cluster mannoside carrying six mannose groups ( $M_6L_5$ ) displayed a subnanomolar affinity for the mannose receptor ( $K_1=0.41\pm0.09$  nmol/L). Preinjection of  $M_6L_5$  (1.2 mg/kg) reduced the clearance of  $^{125}\text{I}$ -TPA in rats by 60% because of specific inhibition of the endothelial cell uptake. The low toxicity of

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M<sub>6</sub>L<sub>5</sub>, combined with its accessible synthesis and high specificity for the mannose receptor, makes it a promising agent to improve the pharmacokinetics of TPA. Blockade of LRP by 39-kD receptor-associated protein (GST-RAP) also inhibited TPA clearance by 60%. Finally, combined preinjection of M<sub>6</sub>L<sub>5</sub> and GST-RAP almost completely abolished reduced liver uptake of TPA and delayed its clearance by a factor of 10.

**Conclusions** It can be concluded that (1) the mannose receptor and LRP appear to be the sole major receptors responsible for TPA clearance and (2) therapeutic levels of TPA can be maintained for a prolonged time span by coadministration of the aforementioned receptor antagonists.

**Key Words:** plasminogen activators • thrombolysis • cluster mannoside • GST-RAP

## ► Introduction

Tissue plasminogen activator is a serine protease that plays a central role in the fibrinolytic system.<sup>1 2</sup> TPA converts plasminogen to plasmin, which degrades blood clot-associated fibrin. The fibrin-specific thrombolytic TPA has proved to be a potent drug in several clinical trials.<sup>3 4 5</sup> Despite its widespread clinical application, the thrombolytic efficacy of TPA is complicated by its rapid clearance from the circulation, and large doses of TPA must be administered.<sup>6 7 8 9 10</sup> The short plasma half-life of TPA (ranging from 1 minute in rats to about 6 minutes in humans) results from a rapid liver uptake of TPA.<sup>6 7 8 9 10 11</sup> In vivo studies on TPA have indicated that at least two different hepatic uptake mechanisms are involved in the clearance of TPA from the circulation, because both parenchymal and endothelial liver cells contribute to the liver uptake of TPA.<sup>7 11 12 13</sup>

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The characteristics of the TPA uptake sites on parenchymal and endothelial liver cells differ markedly.<sup>7 12 14</sup> Uptake by endothelial liver cells is mediated by the mannose receptor, which recognizes the mannose-rich oligosaccharide chain at Asn<sub>117</sub> of TPA.<sup>7 11 12 13</sup> The receptor involved in parenchymal liver cell uptake is not unequivocally identified to date.<sup>7 12 13 15 16 17</sup> In vitro binding studies revealed that TPA may interact with LRP, the asialoglycoprotein receptor,<sup>11</sup> and a novel carbohydrate recognition system.<sup>7 12 13 15 16 17</sup> Warshawsky et al<sup>16</sup> showed that an established LRP antagonist, GST-RAP, reduced the in vivo clearance of TPA. Major efforts have been undertaken to construct TPA variants with prolonged plasma half-lives.<sup>18 19 20 21 22 23 24 25</sup> <sup>26</sup> To circumvent endothelial cell uptake of TPA via the mannose receptor, deglycosylated TPA variants were developed, and the clearance of these variants was significantly reduced.<sup>18 19</sup> Alternatively, deletion of the finger and epidermal growth factor domains also resulted in a significant increase of the plasma half-life,<sup>21 22 23 24 25 26</sup> whereas blockade of the active site of TPA (protease domain) only marginally affected the plasma half-life.<sup>12 26</sup> However, the benefit

in overall thrombolytic activity of these variants was often too low to justify further development as a thrombolytic drug.

Therefore, we pursued an alternative approach to improve the pharmacokinetics of TPA. We investigated whether the in vivo half-life of wild-type TPA can be prolonged by blockade of its clearance. We devised and synthesized a series of high-affinity ligands for the mannose receptor. Combination of the developed mannose receptor antagonist with an LRP antagonist reduced the liver uptake of TPA strongly and prolonged the plasma half-life of TPA 10-fold.

## ► **Methods**

### **Materials**

BSA (fraction V), collagenase (types I and IV), and iodogen were purchased from Sigma Chemical Co [ $^{125}\text{I}$ ]NaI (carrier free) and streptavidin–alkaline phosphatase conjugate were from Amersham. Pronase and DNase I were from Boehringer Mannheim GmbH. Nycodenz was from Nycomed Pharma AS (Oslo, Norway). HEPES was from Merck. Recombinant TPA was from Boehringer Ingelheim GmbH. All other chemicals were of analytic grade. The synthesis of  $\text{M}_6\text{L}_5$  is described in detail elsewhere.<sup>27</sup>

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▼	<a href="#">References</a>

### **Production and Isolation of GST-RAP**

A plasmid (pGEX) encoding for a fusion protein (GST-RAP) of GST and the 39-kD protein or receptor-associated protein (RAP), which was transformed in *Escherichia coli* (DH5 $\alpha$ ), was a generous gift of Dr J. Herz (Dallas, Tex). GST-RAP was produced exactly as described.<sup>28</sup> The potency of GST-RAP to displace trypsin-activated  $^{125}\text{I}$ - $\alpha_2\text{M}$  binding from its receptor was essentially equal to values described in the literature ( $\text{IC}_{50}$ , 1 nmol/L).

### **Isolation of Human Mannose Receptor**

Human mannose receptor was isolated from human placenta after solubilization with Triton X-100 and subsequently purified by affinity chromatography over mannosylated albumin-sepharose according to Otter et al.<sup>29</sup>

### **Biotinylation and Radiolabeling of TPA**

TPA was dialyzed against 0.1 mol/L  $\text{NaHCO}_3$  (pH 8.5) and reacted with *N*-hydroxysuccinimide–activated biotin (Zymed Laboratories Inc) at a ratio of 1 mol TPA to 200 mol *N*-hydroxysuccinimide–activated biotin at room temperature for 3 hours. After reaction, the modified protein was dialyzed against 20 mmol/L Tris buffer, pH 7.4, containing 0.01% Tween-80 (vol/vol).

Recombinant TPA was iodinated by the iodogen method as described, and a specific radioactivity of 3500 to 5000 cpm/ng protein was obtained.<sup>7</sup>



### **Mannose Receptor Binding Assay**

Displacement studies of the binding of biotinylated TPA to isolated human mannose receptor were performed according to the procedure of Otter et al.<sup>29</sup> Plates were coated with 100  $\mu$ L solubilized receptor in loading buffer (pH 7.4) containing 0.02 mol/L Tris-HCl, 5 mmol/L  $\text{CaCl}_2$ , and 0.15 mol/L NaCl at 4°C overnight. Loading buffer supplemented with 0.5% Tween 80 and 0.1% BSA (125  $\mu$ L) was added for 30 minutes at room temperature to minimize aspecific binding of ligand to the wells. The receptor-coated wells were preincubated with the indicated amounts of competitor for 30 minutes at room temperature. Biotinylated TPA (1.5 nmol/L) was added and incubated for 2 hours at room temperature. Streptavidin-alkaline phosphatase conjugate was added subsequently, and the wells were incubated for 1 hour at room temperature. Next, *p*-nitrophenolphosphate was added, the wells were incubated for 4 hours at 25°C, and finally the absorption at 405 nm was monitored with a microplate reader. Wells were washed three times with 0.5% Tween-80 in loading buffer supplemented with 0.5% Tween and 0.1% BSA after each step of the procedure. Uncoated wells were used as a control for aspecific binding of biotinylated TPA to uncoated wells.

### **In Vivo Plasma Clearance and Organ Uptake**

Twelve-week-old male Wistar rats (225 to 275 g) were anesthetized by injection with 20 mg pentobarbital IP. The abdomen was opened, radiolabeled TPA (600  $\mu$ g/kg body wt) was injected via the vena penis, and at the indicated times, blood samples (0.3 mL) were taken with heparinized syringes from the vena cava and liver lobules were tied off. The liver uptake of the injected compound was corrected for the radioactivity in plasma in the liver at the time of sampling.<sup>7</sup>

### **Cell Isolation Procedures**

For determination of the contributions of different liver cell types to total liver uptake, rats were anesthetized and injected with  $^{125}\text{I}$ -labeled TPA via the vena penis. After 10 minutes, the vena porta was cannulated and a liver perfusion at low temperature (<8°C) was started with Hanks' buffer (supplemented with 10 mmol/L HEPES). Parenchymal liver cells, endothelial liver cells, and Kupffer cells were isolated exactly as described.<sup>7</sup> The contributions of the various liver cell types to total liver uptake were calculated as described.<sup>7</sup> As found for a number of substrates, no loss of cell-bound label and/or formation of acid-soluble radioactivity occurred during the low-temperature cell isolation procedure, leading to a quantitative recovery of radioactivity associated with the isolated liver cells compared with the total liver association. This was checked for each individual liver cell isolation by comparison of the calculated liver association (from the relative contributions of the various cell types) and the determined total liver association.

### **Toxicity Studies**

Rats (Wistar, male, 250 g) were anesthetized with ether, and PBS (500  $\mu$ L) or  $\text{M}_6\text{L}_5$  (6.0 mg/kg) in 500  $\mu$ L PBS was injected in the vena penis. At 2 and 24 hours after injection, blood samples (600  $\mu$ L) were taken. Serum levels of alanine aminotransferase, aspartate aminotransferase, and  $\gamma$ -glutamyl transferase were determined enzymatically with Boehringer Mannheim SYS-3

BM/Hitachi 747 enzyme kits. Kinetic determination of lactate dehydrogenase activity in serum was determined on an SYS-3 BM/Hitachi 747 with the Boehringer Mannheim LDH kit. After 24 hours, rats were killed and liver, spleen, and kidney were excised, weighed, and analyzed histologically.

### Data Analysis

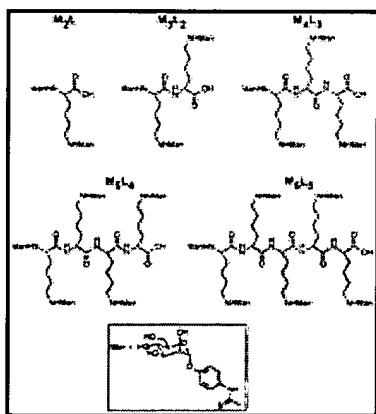
The displacement binding data were analyzed according to a single-site model with a computerized nonlinear fitting program (Prism, GraphPad Software) to calculate the  $IC_{50}$  values.<sup>30</sup> The  $K_i$  was calculated from the corresponding  $IC_{50}$  by the Cheng-Prusoff equation [ $K_i = IC_{50} / (1 + \text{Ligand} / K_d)$ ] and assuming the  $K_d$  of TPA to be 1.0 nmol/L. Pharmacokinetic studies of TPA clearance were analyzed according to a two-phase exponential decay model using the same program. Clearance (Cl) was calculated from the area under curve (AUC) of the plasma decay and the injected dose of TPA according to the equation  $Cl = \text{Dose} / \text{AUC}$ . The significance of differences between means was tested by unpaired two-way Student's *t* test. Significance of the differences in TPA clearance between control and treated rats was analyzed by one-way ANOVA with a Student-Newman-Keuls multiple-comparison post hoc test (Instat, GraphPad software).

## ► Results

### Mannose Receptor Binding Studies

A series of cluster mannosides on a base of an oligolysine backbone was synthesized<sup>27</sup> (for chemical structure see Fig 1□). The cluster mannosides contain an increasing number of mannose residues, and their affinity for the isolated human mannose receptor was tested (Fig 2□). All cluster mannosides completely inhibited the binding of biotinylated TPA to the mannose receptor, and the potency to compete for the binding of TPA increased dramatically with increasing mannose valency. From the inhibition curves, the inhibition constants were calculated. It was found that the inhibition constant of  $M_6L_5$  ( $0.41 \pm 0.09$  nmol/L), which showed the highest affinity for the mannose receptor, was almost  $10^7$ -fold lower than that of mannose ( $4.0 \pm 0.6$  mmol/L).

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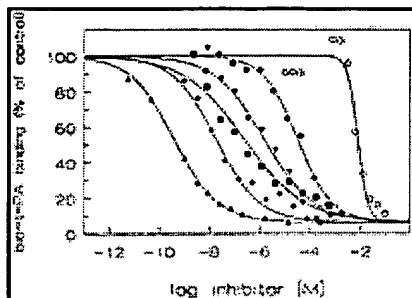


**Figure 1.** Chemical structures of the synthesized cluster mannosides.

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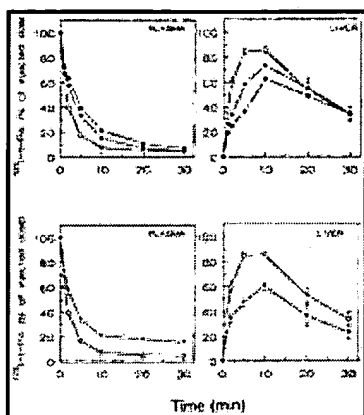
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**Figure 2.** Displacement of binding of biotinylated TPA to the isolated human mannose receptor by cluster mannosides. Competition experiments were performed as follows. Multiwells coated with isolated human mannose receptor were incubated for 2 hours at 25°C with biotinylated TPA (1.5 nmol/L) in the absence or presence of the indicated amount of displacer: mannose (○), M<sub>2</sub>L (●), M<sub>3</sub>L<sub>2</sub> (▼), M<sub>4</sub>L<sub>3</sub> (■), M<sub>5</sub>L<sub>4</sub> (◆), and M<sub>6</sub>L<sub>5</sub> (▲). Binding of biotinylated TPA is expressed as percentage of the control binding of biotinylated TPA (without displacer).

### Effect of M<sub>6</sub>L<sub>5</sub> on the Plasma Clearance and Liver Uptake of TPA

Since TPA is in part cleared from plasma via the liver mannose receptor, we determined the effect of the high-affinity ligand for the mannose receptor, M<sub>6</sub>L<sub>5</sub>, on TPA clearance. In control rats, <sup>125</sup>I-TPA (600 µg/kg) was rapidly cleared from the bloodstream ( $t_{1/2}$ , 1.1±0.1 minutes; Fig 3 □) because of a rapid uptake of TPA by the liver, and a maximum of 86±1.5% of the injected dose was recovered in the liver. Injection of M<sub>6</sub>L<sub>5</sub> 1 minute before <sup>125</sup>I-TPA resulted in a significant and dose-dependent reduction in TPA clearance. At a dose of 0.12 mg M<sub>6</sub>L<sub>5</sub>/kg, the rate of TPA clearance was reduced by 48% (1.9±0.1 and 3.5±0.2 mL/min for 0.12 mg M<sub>6</sub>L<sub>5</sub>/kg and controls, respectively; Fig 4 □), whereas 1.2 mg M<sub>6</sub>L<sub>5</sub>/kg inhibited the clearance for 59% (1.46±0.07 mL/min). Concomitantly, the liver uptake of TPA was delayed, and the maximal liver uptake was reduced to 73±1% and 62.5±1.0% of the injected dose after preinjection of 0.12 and 1.2 mg M<sub>6</sub>L<sub>5</sub>/kg, respectively.

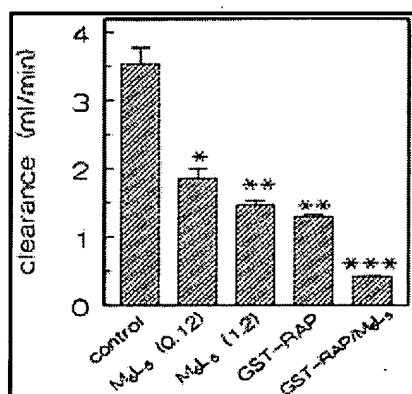
**Figure 3.** Effect of M<sub>6</sub>L<sub>5</sub> or GST-RAP on the plasma clearance and liver uptake of <sup>125</sup>I-TPA. <sup>125</sup>I-TPA (600 µg/kg) was injected intravenously into rats that had been preinjected with 0.12 mg/kg M<sub>6</sub>L<sub>5</sub> (top, ●), 1.2 mg/kg M<sub>6</sub>L<sub>5</sub> (top, ■), 40 mg/kg GST-RAP (bottom, ▼), or PBS (top and bottom, ○). At the indicated times, radioactivity in plasma and liver was determined. Data points are mean±SEM of three (pretreated rats) or eight (control) experiments.



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**Figure 4.** Effect of mannose receptor and LRP antagonists on the clearance of  $^{125}\text{I}$ -TPA. From the plasma clearance data (Figs 3 and 5), TPA clearance (in mL/min) was calculated from the pharmacokinetic parameters area under the curve and injected dose. The level of significance is indicated as \* $P < .05$ , \*\* $P < .01$ , and \*\*\* $P < .001$ .

### Effect of GST-RAP on the Plasma Clearance and Liver Uptake of $^{125}\text{I}$ -TPA

To address the involvement of LRP in TPA clearance, we studied the effect of an established antagonist of LRP,<sup>30</sup> GST-RAP, on the clearance of TPA in the rat. Fig 3 shows that preinjection of GST-RAP (40 mg/kg) strongly affected the pharmacokinetics of  $^{125}\text{I}$ -TPA (600  $\mu\text{g/kg}$ ). At 10 minutes after injection,  $21 \pm 1\%$  of the injected dose still resided in the circulation, and the clearance was reduced significantly, by 63% ( $1.30 \pm 0.03$  and  $3.5 \pm 0.2$  mL/min for GST-RAP-treated and control, respectively; Fig 4). GST-RAP pretreatment led to a delay in liver uptake of  $^{125}\text{I}$ -TPA, and maximal liver uptake was reduced to  $60 \pm 2\%$  of the injected dose.

### Effect of M<sub>6</sub>L<sub>5</sub> and GST-RAP on the Hepatocellular Distribution of TPA

To determine whether the receptor antagonists M<sub>6</sub>L<sub>5</sub> and GST-RAP indeed blocked uptake of  $^{125}\text{I}$ -TPA via the corresponding receptors, we studied their effects on the uptake of  $^{125}\text{I}$ -TPA in

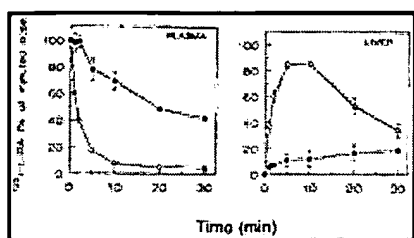
the various liver cell types (Table 1<sup>□</sup>). As described before,<sup>7</sup> parenchymal and endothelial liver cells appeared to be the major cell types responsible for liver uptake of <sup>125</sup>I-TPA in control rats; 55±1.5% of total liver uptake of <sup>125</sup>I-TPA was recovered in parenchymal liver cells, and 40±2% was recovered in endothelial cells. Preinjection of M<sub>6</sub>L<sub>5</sub> (1.2 mg/kg) caused a significant shift in the liver cell distribution profile. Parenchymal liver cell uptake increased significantly, to 71±3%, while at the same time the relative contribution of endothelial cells to <sup>125</sup>I-TPA uptake decreased to 19.5±1% of the total liver uptake. The increase of the relative contribution of parenchymal liver cells was not caused by enhanced uptake per milligram of cell protein. The specific parenchymal liver cell uptake of <sup>125</sup>I-TPA was not influenced by preinjection of M<sub>6</sub>L<sub>5</sub>, in contrast to the specific endothelial cell uptake, which was reduced by 72% (124±5% and 430±40% of injected dose/10<sup>3</sup>/mg cell protein for M<sub>6</sub>L<sub>5</sub>-treated rats and for controls, respectively).

**View this table:** **Table 1.** Contribution of Various Cell Types to the Liver Association of <sup>125</sup>I-TPA: Effect of Preinjection of M<sub>6</sub>L<sub>5</sub> or GST-RAP  
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By contrast, GST-RAP treatment reduced parenchymal cell uptake by 65% (7.6% versus 21±4% of injected dose/10<sup>3</sup>/mg cell protein for GST-RAP-treated and control rats, respectively). Concomitantly, specific endothelial cell uptake was increased by 44% to 619% of injected dose/10<sup>3</sup>/mg cell protein on GST-RAP treatment. Apparently, TPA uptake is partly compensated by an increased uptake by mannose receptor in case the LRP-mediated pathway is blocked. Both GST-RAP and M<sub>6</sub>L<sub>5</sub> preinjection did not significantly affect Kupffer cell uptake of TPA.

### **Effect of Combined Treatment With M<sub>6</sub>L<sub>5</sub> and GST-RAP on the Plasma Clearance and Liver Uptake of <sup>125</sup>I-TPA**

These findings demonstrate that although GST-RAP and M<sub>6</sub>L<sub>5</sub> both affect TPA clearance, blockade of either receptor system is not sufficient to prevent clearance of TPA. Therefore, we treated rats with both M<sub>6</sub>L<sub>5</sub> (1.2 mg/kg) and GST-RAP (40 mg/kg) and determined that the plasma clearance of <sup>125</sup>I-TPA (600 µg/kg) was almost completely blocked (Fig 5<sup>□</sup>). At 10 minutes after injection, 70±7% of the injected dose is still recovered in the plasma, which is significantly more than in untreated controls (8±0.4%), in M<sub>6</sub>L<sub>5</sub>-treated rats (21±3%), or in GST-RAP-treated rats (21±1%). The TPA clearance is reduced almost 10-fold, from 3.5±0.2 mL/min for the control rats to 0.42±0.05 mL/min for the combined treatment (Fig 4<sup>□</sup>). Moreover, liver uptake of <sup>125</sup>I-TPA was almost completely abolished after preinjection with GST-RAP and M<sub>6</sub>L<sub>5</sub>. Only 18.7±0.8% of the injected dose, at maximum, was recovered in the liver, compared with 86±1.5% for controls.



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**Figure 5.** Effect of simultaneous preinjection of GST-RAP and M<sub>6</sub>L<sub>5</sub> on the plasma decay and liver

association of <sup>125</sup>I-TPA. <sup>125</sup>I-TPA (600 μg/kg) was injected intravenously into rats that had been preinjected at 1 minute before TPA injection with PBS (○) or 40 mg/kg GST-RAP plus 1.2 mg/kg M<sub>6</sub>L<sub>5</sub> (■).

At the indicated times, radioactivity in plasma and liver was determined. Data points are mean±SEM of three (treated rats) or eight (control) experiments.

To exclude the possibility that the observed effect of combined treatment with GST-RAP plus M<sub>6</sub>L<sub>5</sub> on TPA clearance resulted from an aspecific effect of GST-RAP and/or M<sub>6</sub>L<sub>5</sub> on hepatic blood flow or receptor-mediated endocytosis in general, we also tested the effect of combined treatment on the *in vivo* kinetics of <sup>125</sup>I-ASOR, which is an established substrate for the asialoglycoprotein receptor. No effect of combined treatment was observed on liver uptake or plasma clearance of <sup>125</sup>I-ASOR. The plasma half-life of ASOR was 0.53 minute in treated and 0.51 minute in untreated rats (data not shown).

### Toxicity of M<sub>6</sub>L<sub>5</sub>

To validate the potential of M<sub>6</sub>L<sub>5</sub> as a therapeutic additive in thrombolytic therapy, we assessed the acute toxicity of M<sub>6</sub>L<sub>5</sub> (Table 2<sup>Ⓢ</sup>). Even at doses (6 mg/kg) 5 to 50 times higher than doses used in this study, M<sub>6</sub>L<sub>5</sub> was essentially nontoxic after single bolus injection. Liver, spleen, and kidney weights remained unaffected, and serum parameters for systemic (lactate dehydrogenase) and liver toxicity (alanine aminotransferase, aspartate aminotransferase, and γ-glutamyl transferase) at 2 hours and at 24 hours after injection were essentially unaltered. Histological analysis of liver did not show any signs of toxicity. We may therefore assume that the toxicity of M<sub>6</sub>L<sub>5</sub> is very low.

View this table: **Table 2.** Toxicity of M<sub>6</sub>L<sub>5</sub> in Rats

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## ► Discussion

The therapeutic effectiveness of the highly potent thrombolytic agent TPA is reduced by its rapid elimination from the bloodstream, which results from an efficient liver uptake. A first approach to improve the pharmacokinetics of TPA has been the construction of TPA mutants that lack those domains responsible

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for hepatic uptake.<sup>18 19 20 21 22 23 24 25 26 31 32 33</sup> We used another, still unexplored, approach and developed a highly specific antagonist for the mannose receptor, which is responsible for 40% of the liver uptake of TPA.

▼ References

In search of high-affinity mannose receptor ligands, we synthesized a series of cluster mannosides that contained two ( $M_2L$ ) to six ( $M_6L_5$ ) mannose residues per cluster molecule. The cluster mannoside that carried two mannose groups ( $M_2L$ ;  $K_i$ , 16  $\mu\text{mol/L}$ ) already displayed a 250-fold higher affinity than  $\alpha$ -D-mannose ( $K_i$ , 4.0  $\text{mmol/L}$ ). The most potent mannoside,  $M_6L_5$ , had an affinity for the mannose receptor of 0.41  $\text{nmol/L}$ , which is substantially higher than that of ovalbumin ( $K_i$ , 290  $\text{nmol/L}$ <sup>14</sup>) or mannosylated BSA ( $K_i$ , 2.2  $\text{nmol/L}$ <sup>34</sup>) and quite similar to that of TPA ( $K_i$ , 0.6  $\text{nmol/L}$ <sup>14</sup>). Previously developed synthetic mannosides—mostly branched oligosaccharides—possessed affinities only in the low micromolar range,<sup>35</sup> which is >1000-fold lower than the affinity of  $M_6L_5$ . The subnanomolar affinity of  $M_6L_5$ , in combination with its accessible synthesis, makes  $M_6L_5$  a promising compound to inhibit mannose receptor-mediated uptake of TPA.

In vivo,  $M_6L_5$  significantly and dose-dependently inhibited the clearance of  $^{125}\text{I}$ -TPA (injected at a therapeutic dose of 600  $\mu\text{g/kg}$ ) by up to 59%. The reduction in liver uptake of TPA by  $M_6L_5$  treatment resulted from a specific inhibition of TPA uptake by endothelial liver cells. This corresponds well with earlier studies showing that the clearance of deglycosylated TPA mutants was retarded by a factor of 3 compared with unmodified TPA.<sup>18 30 35</sup> Blockade of the plasma clearance of TPA could be reduced 2.6-fold on blockade of the mannose receptor by high doses of mannan (20  $\text{mg/kg}$ ) or ovalbumin (80  $\text{mg/kg}$ ).<sup>7 11</sup> These data illustrate that  $M_6L_5$  is 15- to 70-fold more effective than ovalbumin and mannan in the in vivo blockade of TPA clearance via the mannose receptor. Toxicity studies showed that  $M_6L_5$  is tolerated well at doses 5- to 50-fold higher than the doses that were needed to inhibit TPA clearance. No signs of acute systemic or liver toxicity were observed after single injection of 6.0  $\text{mg } M_6L_5/\text{kg}$ . Moreover,  $M_6L_5$  is probably far less immunogenic than mannan or ovalbumin. It can therefore be concluded that the high affinity and specificity of  $M_6L_5$  for the mannose receptor, together with its low toxicity, makes it a valuable therapeutic to improve the pharmacokinetics of TPA.

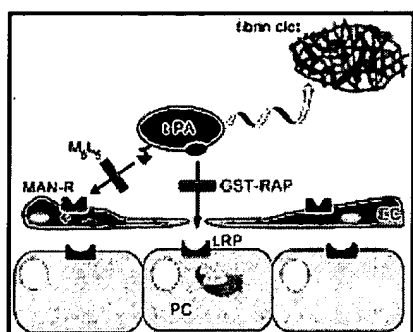
To establish the involvement of LRP in TPA clearance, we quantified the effect of preinjection of GST-RAP (40  $\text{mg/kg}$ ) on TPA clearance. GST-RAP, a widely used antagonist of LRP,<sup>28</sup> appeared to increase the plasma half-life of  $^{125}\text{I}$ -TPA 2.7-fold. Warshawsky et al<sup>16</sup> showed a similar effect of GST-RAP on TPA clearance. In an extension of their study, we show that GST-RAP pretreatment delayed and reduced liver uptake of TPA significantly, by 30%, and the data on the liver cell distribution of TPA show that GST-RAP specifically reduced the uptake by parenchymal liver cells.

The effect of GST-RAP on liver uptake was comparable to that of  $M_6L_5$ . Apparently, neither antagonist can fully block the plasma clearance of TPA or TPA uptake by the liver. The simultaneous blockade of LRP and the mannose receptor by preinjection of GST-RAP and  $M_6L_5$  almost completely abolished liver uptake and at the same time reduced TPA clearance 10-fold. Combined treatment did not affect clearance and liver uptake of another fast-clearing glycoprotein, ASOR, excluding the theory that the blockade of TPA clearance results from aspecific effects of the combined treatment on hepatic blood flow or receptor-mediated endocytosis. The effect of the combined treatment on the clearance of TPA matches very well with the kinetics of TPA reported in rats preinjected with an excess of unlabeled TPA (20 mg/kg).<sup>7 16</sup> In these studies, half of the injected dose of TPA was still present in the circulation at 30 minutes after injection.<sup>7 16</sup> Prevention of the liver uptake of TPA by hepatectomy also resulted in a 10-fold decreased clearance.<sup>6 9 10</sup> Apparently, TPA clearance is prolonged by a factor of 10 by prevention of its liver uptake. Recently, Narita et al<sup>36</sup> reported that the plasma half-life of TPA (10  $\mu$ g/kg) in RAP-overexpressing mice was enhanced to 20 minutes after preinjection of 150 mg ovalbumin/kg body wt. Although this suggested that the mannose receptor and LRP are the sole contributors to liver uptake of TPA, that was not conclusively established. First, ovalbumin blocks not only mannose receptors but also asialoglycoprotein receptors, which was also suggested to be involved in TPA clearance.<sup>11</sup> Second, RAP is a chaperone protein involved in intracellular trafficking of proteins, suggesting that systemic RAP overexpression in mice may also affect other endocytotic pathways that are important for TPA clearance. Most importantly, Narita et al used tracer doses of TPA (10  $\mu$ g/kg, which is 60-fold lower than therapeutic doses). At therapeutic doses of 600  $\mu$ g/kg, alternative TPA uptake pathways may contribute to TPA liver uptake. This study therefore provides additional information that the mannose receptor and LRP are indeed the only major contributors to the liver uptake and rapid clearance of TPA.

In conclusion, we now show that therapeutic levels of plasma TPA can be maintained for a prolonged time span by blockade of both LRP and the mannose receptor-mediated liver uptake of TPA (Fig 6□). The rather unexplored approach to improve the clinical effectiveness of TPA by means of receptor blockade involves the combined application of the mannose receptor ligands used in this study and TPA-specific LRP antagonists. As a result, lower doses of costly TPA will suffice for thrombolytic therapy, and TPA pharmacokinetics will be greatly improved, leading to fewer unwanted side effects. Blockade of LRP-mediated uptake of TPA by GST-RAP requires rather high doses, which qualifies its potential in thrombolytic therapy. However, more specific and potent LRP antagonists may be developed by combinatorial immunoglobulin repertoire cloning,<sup>37</sup> or recently described truncated RAP mutants<sup>38</sup> may be applied for this purpose. Compared with application of new slow-clearing TPA variants, application of one of the above antagonists in thrombolytic therapy offers the advantage that it may improve the thrombolytic activity of wild-type TPA, an acknowledged and successful fibrinolytic agent.

**Figure 6.** Concept for mechanism by which mannose





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receptor and LRP antagonists interfere with TPA catabolism. TPA exposes two domains that interact with mannose receptor on endothelial cells and LRP on parenchymal liver cells, respectively. GST-RAP prevents uptake via LRP, and the newly devised cluster mannoside  $M_6L_5$  prevents mannose receptor-mediated uptake of TPA. Combined therapy totally blocks liver uptake, and subsequently, more TPA is available for the lysis of blood clots. Man-R indicates mannose receptor; PC, parenchymal liver cell; and EC, endothelial cell.

## ► Selected Abbreviations and Acronyms

$\alpha_2M$  =  $\alpha_2$ -macroglobulin

ASOR = asialoorosomucoid

GST-RAP = fusion protein of glutathione S-transferase and  $\alpha_2M$ -receptor-associated protein

LRP = LDL receptor-related protein

$M_6L_5$  =  $N^2$ -[ $N^2$ -[ $N^2$ -[ $N^2, N^6$ -Tris[ $N$ -( $p$ -( $\alpha$ -D-mannopyranosyloxy)anilino)thiocarbamyl]-L-lysyl]- $N^6$ -[ $N$ -( $p$ -( $\alpha$ -D-mannopyranosyloxy)anilino)thiocarbamyl]-L-lysyl]- $N^6$ -[ $N$ -( $p$ -( $\alpha$ -D-mannopyranosyloxy)anilino)thiocarbamyl]-L-lysyl]- $N^6$ -[ $N$ -( $p$ -( $\alpha$ -D-mannopyranosyl-oxy)-anilino)thiocarbamyl]-L-lysine

TPA = tissue plasminogen activator

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